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CELIAC DISEASE (CHRONIC INTESTINAL INDIGESTION)

A SIMPLE, THREE-PHASED, HIGH PROTEIN DIET *

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Very little has been added to our clinical knowledge of chronic intestinal indigestion (celiac disease) since Samuel Gee's [1] paper, in 1888. His lucid description is partly as follows:

It often begins during the second year of life. Signs of the disease are yielded by the faeces; being loose, not formed, but not watery; more bulky than the food taken would seem to account for; pale in color as if devoid of bile; yeasty, frothy, an appearance probably due to fermentation. The pale, loose stools look very much like oatmeal porridge or gruel. . . .

The onset is usually gradual, so that its time is hard to fix. Sometimes the complaint sets in suddenly, like an accidental diarrhea; but even when it is so, the nature of the disease soon shows itself. The patient wastes more in the limbs than in the face, which often remains plump until death is nigh. The belly is mostly soft, doughy, and inelastic; sometimes distended and rather tight. Appetite for food differs. . . .

The course is always slow, whatever be its end; whether the patient live or die, he lingers ill for months or years. Recovery is complete or incomplete. While the disease is active, children cease to grow; even when it tends slowly to recovery they are left frail and stunted.

To regulate the food is the main part of the treatment. Cow's milk is not only not suited, but is the least suited kind of food, nothing more certain. Asses' [2] milk agrees with these patients very well. Starchy foods are unfit. . . . Mutton and beef, raw or very undone, pounded and rubbed through a sieve, should be given from four to six tablespoonfuls daily. . . . No kinds of fruits or vegetables. The diet may seem scanty, but what the patient takes beyond his power of digestion does harm. Carbonate of bismuth and chalk powder may be prescribed. If the patient can be cured at all it must be by diet.

Herter,[3] in a monograph published in 1908, described this condition as "intestinal infantilism." He found a strictly protein diet, consisting mainly of curds, most beneficial, and attributed the definitely therapeutic action of the protein diet to "its influence on the intestinal flora."

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* Received for publication, Dec. 4, 1924.

* (From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital, Chicago, and the Department of Pediatrics, Evanston Hospital.)

1. Gee, S.: On the Celiac Affection, St. Barth. Hosp. Rep. **24**:17, 1888.

2. Asses' milk consists of: protein, 1.8; lactose, 5.5; fat, 1; salts, 0.4; water, 91.3 per cent. Still, G.: Common Disorders of Childhood, **4**:65, 1924.

3. Herter, C.: Infantilism from Chronic Intestinal Infection, New York, 1908.

Heubner,[4] the year following, in a painstaking clinical study, emphasized the importance of a high protein, low carbohydrate and fat diet.

He says: Fat alone is not to be blamed for this condition, as adding skimmed milk to a milk-free diet will cause a relapse. Intolerance for milk-sugar is very marked; buttermilk and malt soup are also harmful. If asses' milk is used, no other carbohydrate or fat should be added. The best diet is an almost exclusively protein one. Eggs, curds of skimmed milk as used by Finkelstein in feeding atrophic infants, and small quantities of lean meat may be fed. Dextrinized carbohydrates, such as zwieback and bread-crusts are best tolerated when very cautiously added after improvement is well under way.

Despite these very definite dietary restrictions, based on clinical observations, chemical, gastric and stool analyses in ten cases, Heubner failed to feed any of his patients as strictly as he advises.

Both Herter and Heubner recognized the existence of numerous gradations of the disease. They differentiated independently two distinct types: (*a*), the mild (rather rare) type is characterized by voluminous, nondiarrheal stools, loss of weight or stationary weight, marked pallor and fatigue; (*b*), the severe (more frequent) type is characterized by very voluminous, foulodored, frothy and acid stools, with periods of diarrhea; the abdomen is distended and the child becomes more or less stunted in growth. More recently, Miller [5] and Brown, Courtney and MacLachlan [6] also grouped their cases according to the severity of symptoms. No clinician has recorded whether the severe cases were mild at first, or whether the severity is dependent on diet alone. Modern textbooks invariably state that the course is chronic; that exacerbations, with extreme losses in weight, are likely to occur from time to time regardless of diet.

In the last few years Miller [5] has written extensively concerning all phases of this chronic disease. He stresses the importance of fat reduction when he says: "work out a diet containing the optimum fat . . . . one on which there will be a satisfactory growth and a complete absence of symptoms." He concludes that: "the modern treatment, although not apparently curative, is very successful." Still [7] prohibits all fresh cow's

4. Heubner, O.: Ueber Schwere Verdauungsinsufficienz beim Kinde jenseits des Säuglingsalters, Jahrb. f. Kinderh. **70**:667, 1909.

5. Miller, R.: Celiac Disease (on Nomenclature), Lancet **2**:806, 1919; On the Celiac and Allied Types of Infantilism, Brit. J. Child. Dis. **18**:11 (Jan.-March) 1921; Treatment of Celiac Disease, Lancet **2**:1099 (Nov. 17) 1923; Pathogenesis of Celiac Disease, Arch. Pediat. **40**:88 (Feb.) 1923. Miller, R., and Perkins, H.: The Nondiarrheic Type of Celiac Disease, Lancet **1**:72 (Jan. 13) 1923.

6. Brown, A.; Courtney, A. M., and MacLachlan, I. F.: Effect of Special High Protein Diets in the Treatment of Chronic Intestinal Indigestion in Children, Brit. J. Child. Dis. **19**:113 (July-Sept.) 1922.

7. Still, G.: On Celiac Disease, Lancet **2**:163, 193, 227, 1918; Celiac Disease, Ed. 4, Common Diseases of Childhood, London, **18**:270, 1924.

milk and says: "Many a case has done well on dried skimmed milk as the main article of diet for several years."

While numerous clinicians, especially Gee, Herter and Heubner, call attention to the importance of diets rich in protein, it remained for Howland [8] to demonstrate clinically the vast difference between a diet rather rich in protein and one nearly exclusively protein. In 1921, after years of careful clinical observations in thirty cases of this disease, he pointed out the marked intestinal intolerance to carbohydrate, analogous to the endogenous intolerance in diabetes. He says:

> Halfway measures are quite unavailing and cause only loss of time which is a serious matter. . . . The dietary treatment may be divided into three stages. First, that with protein milk alone. . . . The diet of the second stage consists of protein milk as a basis reinforced by almost pure protein foods. . . . The third stage, that in which carbohydrates are added, is the really difficult one. The addition must be made very gradually with the most careful observation of the digestive capacity.

He remarks that protein milk, more than any other food is likely to bring satisfactory results.

> It is preferable to buttermilk on account of its somewhat higher caloric value and especially because of the far lower sugar content.

Marriott [9] recommends a quart of skimmed lactic acid milk to which is added the unwashed curd of 2 or 3 quarts of skimmed milk. He uses also calcium caseinate (a commercial brand, Casec and Larosan-Roche) and Larosan with skimmed lactic acid milk. Brown, Courtney and MacLachlan's [6] initial diet for severe cases consists mainly of standard strength protein milk. They add, later on, other protein such as lactic acid milk, curds, meat, cheese and gelatin. In seven severe cases which they so treated they report: "strikingly rapid qualitative improvement, as shown by reduction of distension, improvement in vigor and increase in tissue turgor."

It is nearly universally agreed that properly prepared protein milk is a unique food, for in it are united all of the potential dietary means at our disposal to combat fermentation. A comparison of the percentage composition (Table 1) of Finkelstein's [10] albumin milk and that of whole cow's milk shows the former to be relatively rich in protein; namely, the amount of protein is about the same in both, but the lactose, fat and whey salts are appreciably lower in the protein than in the cow's milk.

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8. Howland, J.: Prolonged Intolerance to Carbohydrates, Tr. Am. Pediat. Soc. **33**:11, 1921.

9. Marriott, W.: Celiac Disease, Abt's Pediatrics, Philadelphia, Vol. 3, 1924, p. 386.

10. Finkelstein, H.: Lehrbuch der Säuglinskrankheiten, Ed. 3, Berlin, Julius Springer, 1924, p. 324.

This low percentage of carbohydrate and fat and the relatively high calcium caseinate and lactic acid content inhibit fermentation, and the fine division of the casein facilitate digestion. The beneficial action of this therapeutic food is more or less curtailed if the casein particles are coarse.

Most of these patients can be taken care of in the home, if a proper diet is simply and accurately prepared. The preparation of an ideal protein milk in the home is extremely difficult, not only on account of

TABLE 1.—*Percentage Composition of Whole Milk, Finkelstein's Standard Protein Milk, and Powdered Protein Milk.*

Constituents	Protein	Lactose	Butterfat	Salts	Calories per Ounce
Whole milk	3.5	4.7	4.0	0.7	21
Standard protein milk	2.7	1.4	2.2	0.5	11
Powdered protein milk	38.0	24.0	27.0	5.0	150

TABLE 2.—*Summary of Cases.*

No.	Name	Sex†	Age: At Onset, Mo.	Age: When Protein Diet Was Begun	Hemoglobin, per Cent. (Dare)	Weight in Pounds When Protein Diet Was Begun	Average (Normal) Weight in Pounds	Gain in Pounds*: In 3 Mo. of Treatment	Gain in Pounds*: In 6 Mo. of Treatment	Remarks
2	W. F.	♂	16	18 mo.	45	16½	23	1½	3¼	Intercurrent pertussis and parotitis; mother's care
3	A. J.	♂	14	22 mo.	56	16¼	23	1¾	5¾	Hot weather, extreme anorexia; practical nurse
4	D. J.	♀	26	5¾ yr.	45	22½	44	8¾	14	Walked alone first time 3 months after treatment; hospital ward 3 months, then mother's care
5	A. M.	♀	15	20 mo.	55	18	23	5	11	Mild type; trained nurse
6	C. M.	♀	15	18 mo.	52	18½	22	6	8	Early case; intercurrent pyelitis, bronchitis; trained nurse and mother's care
7	M. S.	♀	14	22 mo.	45	14¼	22	9¼	14½	Severe type; trained nurses
Approximate average			17		50	17¾	26	5½	9½	Three months in bed

* The average (normal) child of this age gains 3 pounds in six months.
† In this column, ♂ indicates male; ♀, female.

the numerous pitfalls in its preparation, but the quality of milks and the variable acidity of buttermilks often effect wide variations in the finished product. To make skimmed milk curds and skimmed lactic acid milk daily in the home also requires skill, patience and time. As many of these children are 2 or more years old, it is rather impractical to feed them the required amount [11] of standard strength protein milk for weeks

11. Finkelstein uses from 180 to 200 gm. of standard strength protein milk per kilogram of body weight daily for infants with dyspepsia.

or months. Howland's excellent hospital results with standard protein milk and the theoretical and practical reasons before noted prompted, in 1921, a trial with powdered protein milk in the treatment of this disease.

I [12] have used various powdered protein milks quite extensively since 1916, for normal as well as for sick infants. As a prophylactic food in the artificial feeding of infants, weighing under 10 pounds (4,535 gm.), gratifying results were usually obtained when from 3 to 5 per cent. of carbohydrate was added. At that time it was found that the optimum amount of powdered protein milk for a day's supply approximated in level packed tablespoonfuls the number of pounds the infant weighed. Thus, a 6 pound (2,727 gm.) infant usually throve on six level, packed tablespoonfuls; a 9 pound (4,082 gm.) infant required about nine level, packed tablespoonfuls of powdered protein milk in twenty-four hours. In the present work, the level, packed tablespoonful again served as the unit of measure in the daily preparation of the food. It has been our experience that any of the established powdered protein milks may be used in the preparation of a satisfactory protein milk of any concentration desired.

Our results with powdered protein milk as the essential diet in the three-phased, high protein diet, coincide with the findings of Howland and of Brown, Courtney and MacLachlan. It substantiates the theory that the course of this disease can be definitely influenced by diet, and that exacerbations can usually be avoided if the proper regimen is consistently adhered to. The rapidity of the gains in weight (see charts), the accuracy, simplicity and concentration of the diet here advocated make it ideal for the home treatment of this, until rather recently, obstinate and recurrent intestinal disorder.

During the first phase, protein milk is the exclusive diet. The initial twenty-four hour diet should consist of several level packed tablespoonfuls of powdered protein milk less than the number of pounds the child weighs. The proper amount of powdered protein milk is mixed with a quart (more or less) of warm (not hot), sterilized water. It may be sweetened with from one-fourth to 1 grain (0.065 gm.) of saccharin. The mixture is passed several times through a fine sieve (thirty-six wires to the inch). It is then divided into four parts, and placed in the refrigerator until used. The food, gently warmed just before serving, is given from a large holed nipple, spoon, cup or dropper at 6 or 7 a. m., 10 or 11 a. m., 2 or 3 p. m. and 6 or 7 p. m. The long night interval is important, for it reduces to a minimum bacterial invasion and growth in the upper part of the small intestine. If anorexia is extreme, a pinch of fat-free cocoa may be boiled in the water before the protein milk is added. A few

12. Sauer, L.: Powdered Protein Milk as a Prophylactic Food, Arch. Pediat. 39:3 (Jan.) 1922.

drops of vanilla extract or of carmin solution sometimes make the food more tempting. Coercion may be necessary the first few days. The child may take the food more readily in strange surroundings, such as a hospital ward. The number of tablespoonfuls of protein milk powder should be increased about 2 tablespoonfuls every five or seven days. The appetite, age and degree of emaciation are factors which should determine the rate of food increase. This may usually be done regardless of the quality of the stools, for improvement in the general condition and weight increase often begin weeks before the stools are typical "soap stools." The food should thus be gradually increased until the number of tablespoonfuls approximates the theoretic number of pounds the child should weigh for his height. Occasionally (in stunted, older children) the number of tablespoonfuls must be increased until it approaches the theoretical number of pounds the child should weigh at that age. The amount of water in the formula may be decreased or increased to 40 ounces (1,183 cm.). When emaciation is pronounced, turgor much reduced, if there has been a persistent diarrhea, or if signs of tetany are present, Ringer's solution [13] should be used in place of the plain water in the preparation of the food; or 4 or more ounces (sweetened, if necessary, with saccharin) may be given twice daily for several weeks. The anemia usually improves rapidly if iron citrate (1 or more grains) is given intramuscularly two or more times weekly for a month. Precipitated chalk (10 grains added to each feeding) seems to lessen intestinal fermentation and abdominal distension. The first phase is adhered to until the stools, distention and appetite show distinct improvement. It should never be less than two weeks, usually three or four weeks will suffice; in exceptionally chronic cases two or more months may pass before repair of the disturbed intestinal function has become sufficient for additions to the diet. Rigid adherence to the protein diet will usually insure an increase in tolerance.

During the second phase protein milk remains the essential diet, but it is supplemented with almost pure protein foods, such as curds of buttermilk or of machine skimmed milk, scraped lean beef, tongue and egg. These additions must be made very cautiously and the quantities gradually increased from week to week. The increase in the powdered protein milk continues automatically as outlined under the first phase, and such auxiliaries as cod liver oil (from 20 drops to 2 teaspoonfuls twice daily), orange juice (from ¼ to 1 ounce [7.5 to 30 c.c.]), powdered spinach (from 1 to 3 teaspoonfuls) and syrup of ferrous iodid (from 5 to 20 drops daily) may be gradually included in the daily routine.

13. Ringer's solution (sodium chlorid 7.0, potassium chlorid 0.1, calcium chlorid 0.2, distilled water ad 1000.) can be conveniently prepared by dissolving a Ringer tablet in a quart of boiled water.

As the patients usually thrive during this phase of the diet without exacerbations, even during hot weather, it should be adhered to until the weight approximates or exceeds the theoretical weight for height. The rapidity of improvement depends on the rigidity of the dietary regimen, duration and severity of the disease, age of the child and season of the year.

During the third phase, carbohydrates, at first dextrinized flours (patent barley flour, flour ball or imperial granum), also arrowroot crackers, finely rolled zwieback or toasted white bread are cautiously added. This change in the diet should never be attempted within the first six weeks of treatment; in severe cases about the third or even the fourth month is usually early enough. Small quantities (from ½ to 1 ounce) of dextrose, dextrimaltose or corn syrup are often well tolerated. Intercurrent parenteral infections, such as pyelitis, bronchitis, and so forth, may be accompanied by a decreased carbohydrate tolerance. If abnormal stools, anorexia, distention or weight loss recur, the carbohydrates should be omitted for several weeks or months longer; that is, the diet should revert to the second phase, or, if necessary, to the first phase until the alimentary tolerance for carbohydrates has improved.

RULES FOR THE CARE AND FEEDING OF CELIAC DISEASE PATIENTS

1. Hospital care is obligatory, if proper nursing care and cooperation cannot be obtained in the home.

2. Patients should be kept in bed until the weight exceeds by several pounds the child's maximum weight before the illness began.

3. Extremes in room and outdoor temperatures must be avoided; the bedding and clothing should be suitable for the season of the year.

4. This simple, high protein (low carbohydrate and fat) diet consists of three phases: (1), concentrated protein milk exclusively; (2), protein milk with other protein foods (curds of buttermilk or of skimmed milk, buttermilk, eggs, lean meat and boiled tongue); (3), same as the second phase with the cautious addition of dextrinized starches (flour ball, patent barley flour, imperial granum, arrowroot crackers); then finely rolled zwieback or toast; ultimately, powdered spinach and sugars (dextrose, dextrimaltose or corn syrup).

5. The number of calories must be ample to ensure a continuous gain in weight (from 45 to 60 or more calories per pound in twenty-four hours). At first the number of level, packed tablespoonfuls of powdered protein milk should approximate the number of pounds the child actually weighs; then gradually to approach the theoretical number of pounds the child should weigh for his height; in much retarded infants it may be necessary ultimately to use as many tablespoonfuls as the child should weigh for his age.

6. The tolerance for carbohydrate and fat should never be overstepped; fresh cow's milk, cream, butter and meat fat must be omitted for many months; if exacerbations occur, they should be omitted for years.

7. Anorexia, abdominal distention, diarrheal or foamy stools necessitate the omission of carbohydrates, fats, fruit, vegetable and cod liver oil; after an interval of weeks or months, they may again be cautiously added.

8. In exacerbations without apparent dietary or climatic cause, parenteral infections should be searched for, as tolerance decreases during such intercurrent diseases as pyelitis, pertussis and bronchitis.

To contrast the result with the liberal diet and the three-phased, high protein diet advocated in this paper, the following cases are reported:

REPORT OF CASES

CASE 1.—R. V., a boy, aged 3½ years, was seen for the first time Sept. 3, 1920. He had been suffering for two years with celiac disease. The present exacerbation was of several months' duration, during which he lost about 9 pounds (4,082 gm.) in weight. The appetite was poor, and the child had not walked for several weeks. The weight was always below the average, being about 17 pounds (7,711 gm.) at 1 year, 21 pounds (9,525 gm.) at 2 years and 27 pounds (12,246 gm.) at 3 years. The family history was of no importance.

Physical Examination.—The boy was frail, anemic, infantile. The abdomen was very prominent and there was movable dulness; the liver and spleen could not be palpated. Chvostek's sign and carpopedal spasm were present; the patellar reflexes were normal. The child could sit, but was too weak to stand or walk. The weight was 18½ pounds; the height, 30 inches (76 cm.); hemoglobin, 45 per cent.; Pirquet test negative; the stool was gray, large and semiformed and contained mucus and curds; the diagnoses were: chronic intestinal indigestion (celiac disease), rickets, tetany and anemia. The treatment was a quart of skimmed, boiled milk, soda crackers, Ringer's solution and precipitated chalk.

In October, the child's weight was 19 pounds (8,600 gm.); hemoglobin 40 per cent.; abdomen tense; ascites increased; temperature 99.2 F.; cough, râles, but no dulness. One hundred and fifty cubic centimeters of citrated blood was given intramuscularly; the diet was changed to curds in skimmed, boiled milk, gelatin and lean scraped beef.

November, 1920. The weight was 19¼ pounds (8,618 gm.); no ascites; appetite and strength improved, proteins of diet increased.

January, 1921. The child was now aged 4 years; the weight, 23¼ pounds (10,886 gm.); height, 32 inches (81 cm.); hemoglobin 50 per cent.; the patient walked alone and the condition had improved.

March, 1922. The child was aged 5¼ years; weight 24 pounds (10,909 gm.); height, 34 inches (86 cm.); hemoglobin, 30 per cent. The mother put the child on a general diet, including cream, butter, bacon, ice cream, bread, cereal and candy. Diarrhea, weakness, prominence of abdomen and anorexia soon developed. The clinical picture resembled that of September, 1920. The following diet was ordered: Powdered protein milk, 18 (20, 22, 24) level tablespoonfuls; water, 36 ounces (1,020 gm.); saccharin, 1 grain (0.065 gm.); divided into four feedings; and increased as outlined every five days.

During the following months improvement was rapid, in spite of the fact that the child passed through an attack of pertussis.

In August, 1922, while in the country, he again received a liberal diet. Within a week a severe exacerbation occurred. He again lost much weight and could not walk.

September, 1923. The child was aged 6 years; the weight, 38 pounds (17 kg.); height, 35 inches (88 cm.) Measles developed, and the protein milk diet was resumed; there was no exacerbation.

May, 1924, the child was aged 7 years; the weight was 39 pounds (17.7 kg.); the height 37 inches (93 cm.), hemoglobin, 50 per cent. The appetite decreased after the protein diet was discontinued. The stools increased in volume and

Fig. 1 (Case 1).—R. V., aged 7, with his sister, aged 3½ years.

were often frothy and offensive. The photographs show the patient at the age of 7 years. At his side is his sister of the same height, but of only half his age.

The diagnosis of chronic intestinal indigestion (celiac disease) was based on the history, physical examination (including weight and height for age determinations) and the stool analysis.

Case 2.—W. F., a boy, was born Oct. 21, 1921, weighing 7½ pounds (3,409 gm.). At 15 months he walked, had eight teeth and weighed 23 pounds (10.5 kg.). At this time, while on a rational diet, an obstinate diarrhea developed with a weight decrease of 2 pounds (907 gm.). Soon thereafter the stools appeared remarkably large, were often foamy, gray, oily and offensive. The weight decrease became even more marked during the last month.

Physical Examination.—May 15, 1923, the child appeared very ill. He was too weak to sit or stand; he was pale and the tissue turgor was much reduced. The abdomen was very prominent, but not tympanitic. There was no free fluid; no abdominal masses could be palpated, the liver and spleen were not palpable. The superficial glands were not enlarged. There was definite beading of the ribs. Heart, lungs and throat were normal. The weight was 17 pounds (7,711 gm.); height, 27½ inches (69 cm.) The temperature and urine were normal; hemoglobin, 45 per cent. (Dare); Pirquet test was negative; the stool was very

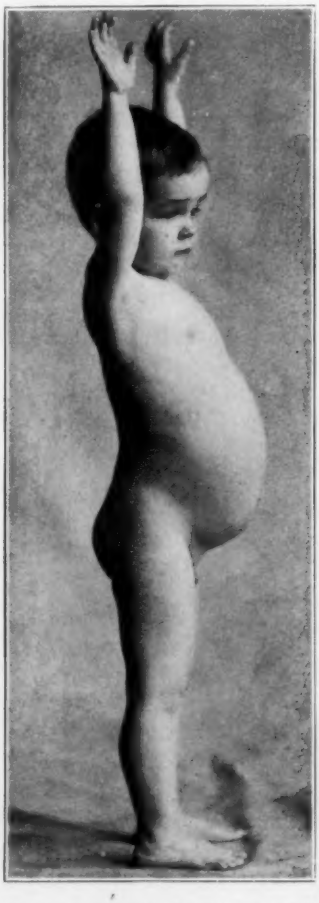

Fig. 2.—Side view of the same patient, showing the abdominal protuberance.

voluminous, foamy, greasy and contained starch. The diagnosis was chronic intestinal indigestion (celiac disease).

The treatment was powdered protein milk, 16 (18, 20) level tablespoonfuls; water, 32 ounces (1,020 gm.); saccharin, 1 grain. This was divided into four feedings; increased as outlined every five to seven days. Iron citrate was given intramuscularly, and precipitated chalk four times daily was given for several months.

Later in May as the child refused to take the protein milk, no matter how disguised, the curds of two (later three and four) quarts of buttermilk were

mixed with a pint or more of junket made of skimmed milk. In June, the patient passed through a severe attack of pertussis. The abdomen increased in size and the stools were large and offensive. The child again refused protein milk; lean meat and egg yolk were added. In October he was aged 2 years; the weight was 19 pounds (8 kg.) (a pound less than at 1 year), and the child began to walk again.

In October, 1924, the weight was 28½ pounds (12 kg.). During the last year he gained about a pound a month. His diet always included an excess of proteins, but not much protein milk.

CASE 3.—A. J., a boy, aged 17 months, came first under observation July 15, 1921. He was suffering from a severe intestinal disturbance and had lost 4½ pounds (2,050 gm.) during the preceding four months. When not diarrheal, the stools were frequently of the consistency of oatmeal porridge, and voluminous and offensive. The appetite had been extremely poor for months and the child

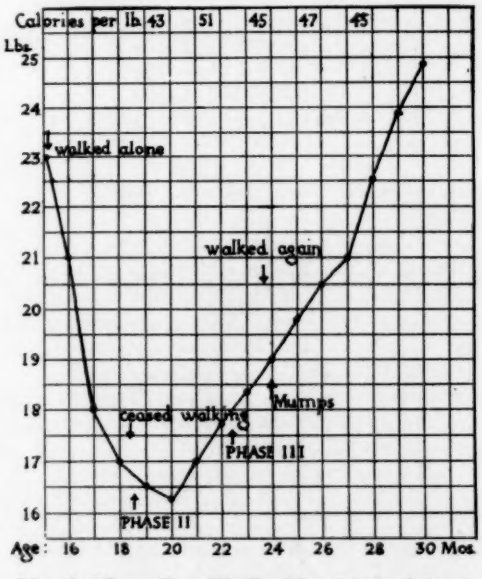

Fig. 3 (Case 2).—W. F. Monthly weight chart.

was very weak. The family history was negative. His early progress was quite normal. He weighed 19 pounds (8.6 kg.) at 1 year. The diarrhea, anorexia and weight decrease began at the age of 14 months.

Physical Examination.—The child appeared small for his age. He was pale and could not sit, stand or walk. The tissue turgor was reduced. The fontanel admitted three finger tips; there were eight teeth; the abdomen was very prominent and tense, but not tympanitic. There was no movable dulness and the liver and spleen could not be palpated. The heart, lungs and throat were normal. The superficial glands were not enlarged; the reflexes were normal. The child weighed 16¼ pounds (7 kg.); his height was 26½ inches (66 cm.); hemoglobin, 56 per cent. (Dare); Pirquet test was negative; the stool was frothy, gray, acid and contained starch; diagnosis: chronic intestinal indigestion (celiac disease). The treatment was powdered protein milk, 12 (14, 16, 18) level tablespoonfuls; water, 32 ounces; saccharin, ½ grain (0.032 gm.). This was divided into four feedings, and increased as outlined every three days. Iron citrate was given hypodermically, and precipitated chalk was added to each feeding.

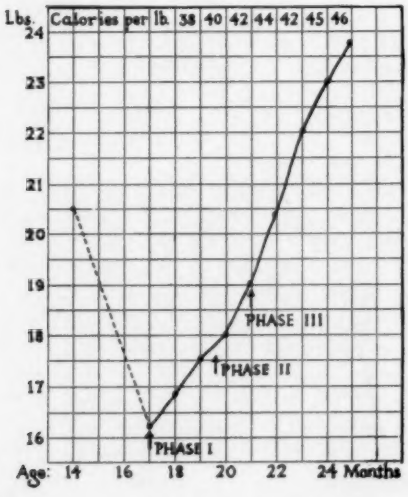

Fig. 4 (Case 3).—A. J. Monthly weight chart.

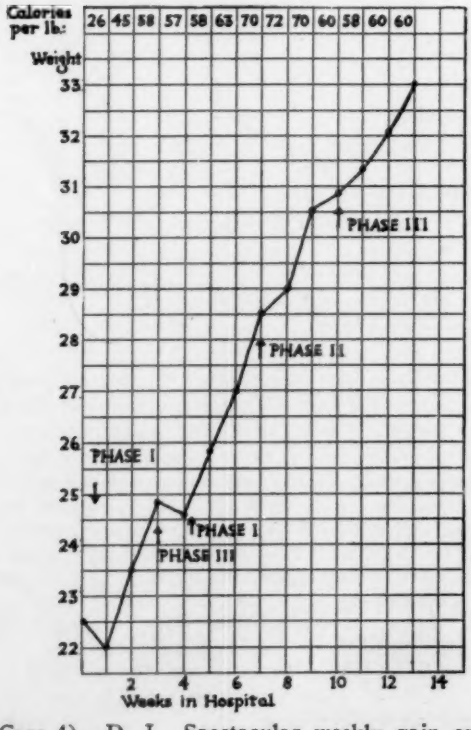

Fig. 5 (Case 4).—D. J. Spectacular weekly gain on protein milk.

The anorexia remained during several weeks of extremely hot weather.

In September the protein milk formula was resumed with the advent of cooler weather. The abdominal distention soon decreased and the strength and weight improved. In October the protein milk powder was increased to twenty-four level tablespoonfuls, and lean beef, boiled tongue and egg were gradually added. In December as improvement continued, patent barley flour, rice flour, arrowroot crackers and toast were gradually added.

The child continued to thrive during the following year on a diet rich in milk proteins. At the age of 4 years the weight and height were scarcely below the average for his age, although he was still rather anemic.

CASE 4.—D. J., a girl, was aged about 5¾ years when first seen, Nov. 8, 1923. She had been suffering with a chronic, severe intestinal disturbance with intermittent diarrhea for several years. The present attack began in July. Since then she lost about 5 pounds (2,267 gm.). The stools were often foamy, and blood was occasionally present. Anorexia had been extreme for months. She could sit and stand, but had never walked alone.

The family history was negative. The birth, Jan. 2, 1918, was normal (the child weighed 6½ pounds). She weighed 17 pounds (7 kg.) at 1 year; 20 pounds (9 kg.) at 2 years and about 26 pounds (11 kg.) at 5½ years.

Physical Examination.—This girl was stunted for her age. She could not walk and was extremely pale. Examination of the heart, lungs and throat was negative. The abdomen was prominent; there was no movable dulness. Her weight was 22½ pounds (10 kg.); height, 34 inches (86 cm.); hemoglobin, 45 per cent. (Dare); Pirquet test was negative; the stools were voluminous, foamy, gray and free from starch; the diagnosis was chronic intestinal indigestion (celiac disease); the treatment was powdered protein milk, 18 (20, 22, 24) level tablespoonfuls; water, 32 (36, 40) ounces; saccharin, ½ grain. This was divided into four feedings and increased as outlined every five days. Iron citrate was given intramuscularly daily; Ringer's solution by mouth twice daily; precipitated chalk in each feeding for three months.

The child relished the food and often begged for more. As soon as the food was sufficiently increased, the weight and general condition improved. The stools and abdomen appeared quite normal within three weeks. A deviation in diet was attempted for a week. The same number of calories were supplied, but only half in the form of protein milk. The deficit was made up with boiled, skimmed milk, and an ounce of well cooked cereal. The reaction to this change in diet was almost immediate, the stools again became voluminous, the abdomen prominent and there was a loss of 3 ounces (85 gm.) in weight (see Chart 5). When the diet again consisted exclusively of protein milk, the weight and intestinal condition immediately improved. Scraped beef was added to the daily diet during the seventh, an egg during the eighth and orange juice during the ninth week of treatment. During the tenth week, 30 gm. of dextrose (anhydrous glucose), and during the following week 30 gm. of flour ball were added. During the succeeding weeks these were doubled without harmful effect. The strength and weight of the patient continued to improve. She walked alone for the first time in her life the tenth week of dietary treatment. During the first three and one-half months of protein diet, the hemoglobin increased 12 per cent., the weight 12 pounds (5,555 gm.) and height 2½ inches (7 cm.). She gained during these 105 days one and one-half times as much weight as she did between her second and fifth years. For weeks the diet consisted nearly exclusively of from thirty-five to forty level tablespoonfuls of protein milk.

August, 1924, the weight was 40 pounds (18 kg.); hemoglobin, 68 per cent. (Dare); general condition good; abdomen, soft; bowels, normal; appetite, good. Powdered protein milk still constituted a major portion of her diet. Diet (three meals daily), powdered protein milk, 24 level tablespoonfuls; water, 20 ounces; saccharin, ½ grain. This was mixed and divided into three parts; also skimmed

milk, 32 ounces; imperial granum, 8 level tablespoonfuls; sugar, 1 level teaspoonful; corn syrup, 6 tablespoonfuls; this was boiled for one hour and divided into three parts.

CASE 5.—A. M., a girl, aged 20 months, came first under observation June 21, 1923. She had not gained in weight for several months, had had intermittent diarrhea for some time and was suffering from anorexia and abdominal distention. The family history was negative.

Physical Examination.—This patient appeared like a child only half her age. She was pale and small but not emaciated. She could sit, but could neither

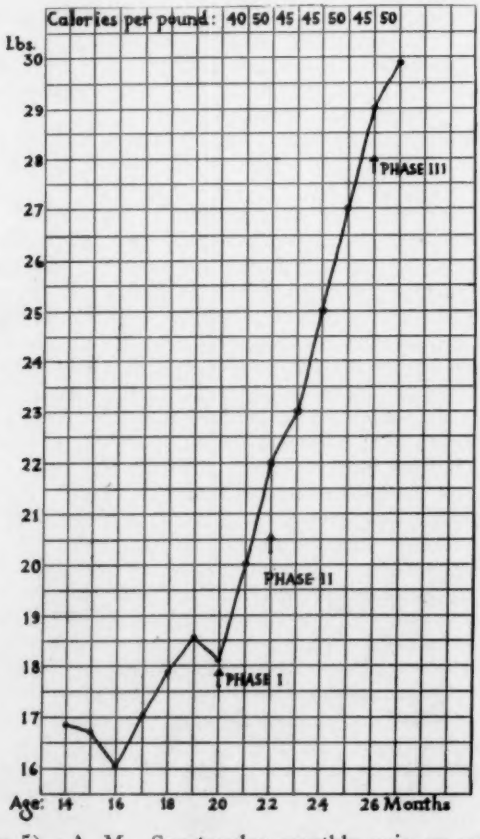

Fig. 6 (Case 5).—A. M. Spectacular monthly gain on protein milk.

stand nor walk. Examination of the heart, lungs and throat was negative. The abdomen was prominent, the liver and spleen were not palpated. The weight was 18 pounds (8 kg.); height, 29 inches (73 cm.); hemoglobin, 55 per cent. (Dare); Pirquet test negative; the stool was gray, voluminous, oily and offensive; the diagnosis was chronic intestinal indigestion (celiac disease), and the treatment was powdered protein milk, 16 (18, 20, 22) level tablespoonfuls; water, 30 ounces; saccharin, ½ grain. This was divided into four feedings; increased as outlined every five days.

July, 1923, the weight had increased two pounds; the stools were nearly normal. The abdominal distention had decreased; the child was stronger and had

a good appetite. The protein milk was increased to 24 level tablespoonfuls, and 1 egg was added to the diet; phosphorized cod liver oil and orange juice were added.

In October, the diet had not been changed for three months. There had been no further intestinal disturbance. The gain in weight had been very rapid (Chart 7). The protein milk, lean meat and egg were increased.

December 1, 3 (4, 5) tablespoonfuls corn syrup and a piece of toast were added.

May, 1924, the child was aged 33 months; the weight was 36 pounds (16 kg.); height, 37 inches (91 cm.); diet, 1,500 calories, as follows:

Breakfast: Powdered protein milk, 8 level tablespoonfuls, 200 calories; dextrimaltose, 3 level tablespoonfuls, 100 calories; fruit, 100 calories; toast, 1 full slice, 100 calories.

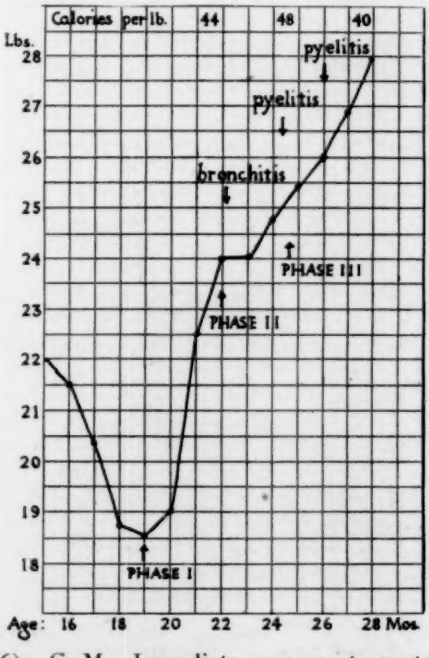

Fig. 7 (Case 6).—C. M. Immediate response to protein milk diet.

Dinner: Powdered protein milk, 8 level tablespoonfuls, 200 calories; dextrimaltose, 3 level tablespoonfuls, 100 calories; vegetable, 100 calories; egg or meat, 100 calories.

Supper: Powdered protein milk, 8 level tablespoonfuls, 200 calories; dextrimaltose, 3 level tablespoonfuls, 100 calories; 1 orange, 100 calories; toast, 1 full slice, 100 calories.

There had been no illness. In the year the weight of the child increased 18 pounds (8 kg.), the height, 6 inches (15 cm.).

September, the child was aged 3 years; her weight was 38 pounds (17 kg.). Stools, and so forth, were excellent.

CASE 6.—C. M., a girl, aged 18 months, come first under observation Aug. 29, 1923. She had been suffering with an intermittent diarrhea for several months, during which time she grew pale and lost over 2 pounds (1 kg.). The family

history was negative, and the early progress of the child was normal. She was born at term (weight, 7¼ pounds). She weighed over 20 pounds (9 kg.) at 1 year. She walked at 14 months, at which time an obstinate colitis with blood and mucus in the stools developed. After recovery from the intestinal upset, pus was found in the urine. She became too weak to walk and the stools were often voluminous, gray, oily and of the consistency of porridge.

Physical Examination.—The body was thin, but not emaciated. Examination of the heart and lungs was negative. The abdomen was prominent; there were

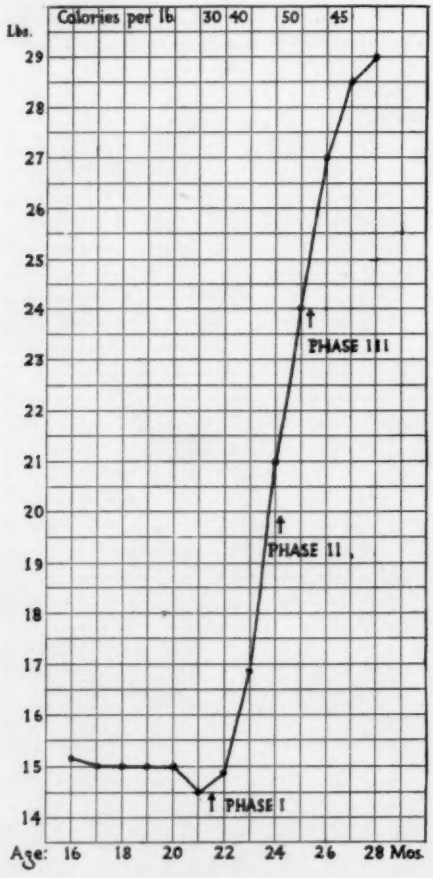

Fig. 8 (Case 7).—M. S. Spectacular monthly gain on protein milk.

no palpable masses; the liver and spleen could not be felt. The weight was 20 pounds (9 kg.); height, 28 inches (71 cm.); hemoglobin, 52 per cent. (Dare); Pirquet test negative; the stool was very voluminous and frothy and contained starch; the urine was normal; the diagnosis was chronic intestinal indigestion (celiac disease). As the child's condition was fairly good, the following diet was tried: skimmed milk, 32 ounces (850 gm.); calcium caseinate, 1 envelope; dextrimaltose, 3 level tablespoonfuls. This was boiled for five minutes in a single boiler, then divided into 4 feedings. The curds of a quart of buttermilk were given daily; also precipitated chalk and iron citrate injections.

In September, there was no improvement; the stools were often foamy, large in quantity and offensive. The abdomen became more distended, the pallor more pronounced, the appetite poor and the weight decreased to 19 pounds (8 kg.).

In October, the weight was 18½ pounds (8.3 kg.); the stools showed no improvement. The following diet was prescribed: Powdered protein milk, 16 (18, 20, 22) level tablespoonfuls; water, 32 (36, 40) ounces; saccharin, 1 grain. This was divided into 4 portions and increased as outlined every five days.

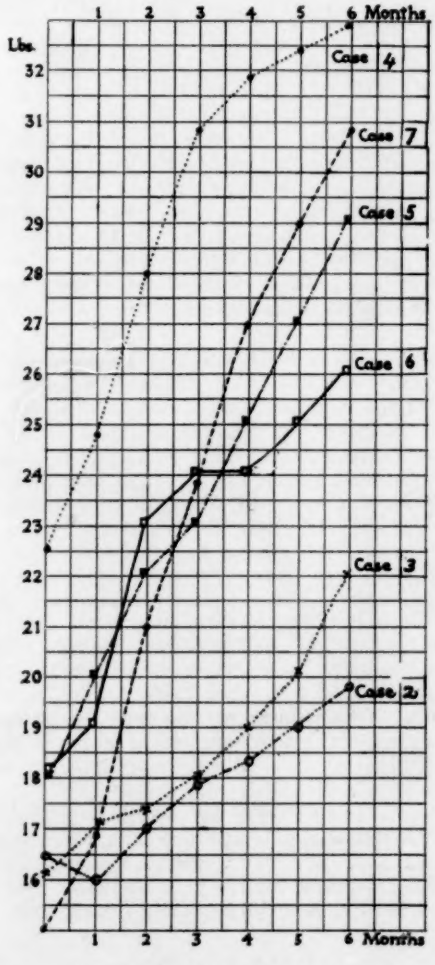

Fig. 9.—Synoptic monthly weight chart for the first six months of treatment in Cases 2 to 7.

In November, the stools, abdomen and appetite were much improved. There was increase in weight. Lean beef, egg, powdered spinach and cod liver oil were added.

In December, increased lean beef; egg and rice flour were added. The stools became more voluminous, but otherwise appeared normal.

In January, 1924, bronchitis with a temperature of 101.5 F. developed, which lasted for about a week. The stools became offensive; the abdomen somewhat

distended and the weight remained stationary for several weeks. The carbohydrates were omitted for a few weeks and were then cautiously resumed.

In February, fever; examination of the patient was negative; the urine contained pus. The stools, abdomen and appetite were not good. Sodium citrate therapy was instituted. The food was temporarily reduced.

December, the child's general condition was excellent. The weight, 30 pounds (13 kg.), equaled that of the average child; the height was scarcely below the average; the hemoglobin was 72 per cent.

COMMENT.—This was an incipient case of the severe type of the disease; the child got worse on skimmed, boiled milk, but improved rapidly on the protein milk diet. She gained 9 pounds (4 kg.) in eight months, and had intercurrent bronchitis and pyelitis with slight exacerbations of the celiac disease.

CASE 7.—M. S., a girl, aged 22 months, came first under observation June 26, 1921. She was suffering from a chronic, severe intestinal disturbance. She weighed 14¾ pounds (6.6 kg.) 1¾ pounds less than at 6 months of age. The family history was negative. Her early progress was quite normal. She was born Aug. 16, 1919; weight, 5¾ pounds (2,267 gm.). At 6 months she weighed 16½ pounds (7.5 kg.) and could sit alone. At 14 months the present trouble began. The very offensive stools were often voluminous, gray and oily. Diarrheal spells, lasting a week or more, occurred from time to time and the weight decreased. The abdomen increased in size, and the child became very weak.

Physical Examination.—The body was very pale and thin. The child could not sit alone. Examination of the heart and lungs was negative. No abnormal masses could be felt; the liver and spleen were not palpable. The weight was 14¾ pounds; height, 27 inches (68 cm.); hemoglobin, 45 per cent.; white blood cells, 11,200; Pirquet (human and bovine) tests were negative. A diagnosis of chronic intestinal indigestion (celiac disease) was made. Treatment given was powdered protein milk, 12 (14, 16, 18, 20) level tablespoonfuls; water, 32 (36) ounces; saccharin, 1 grain. This was divided into 4 feedings and increased as outlined every five days. Iron citrate was given intramuscularly three times weekly; precipitated chalk four times daily in the food for six weeks.

In October, the phenomenal response to the protein milk diet can be seen from the weight chart (Chart 8). In three months the child gained 9¼ pounds (4,082 gm.); the hemoglobin increased to 62 per cent.; the abdomen was scarcely distended, the child was quite lively and could walk with assistance. The diet, besides 24 level tablespoonfuls of protein milk powder, now included curds of 2 quarts of buttermilk, 1 tablespoonful of lean meat and an egg. Then rice flour, arrowroot crackers, powdered spinach and small pieces of toast were gradually added to the diet. She gained 3½ inches (10 cm.) in height during the first year of treatment.

At the age of 3 years she was above the average weight for her age. Her diet at that time included a pint of skimmed, boiled milk, meat, eggs, vegetables, fruit, toast, crackers and a cup of curds daily. Sugars and fats were never added, and only small quantities of cooked cereals were allowed. She has never had an exacerbation of the intestinal disturbance during the last three years.

CONCLUSIONS

1. All students of this disease advocate a high protein, low carbohydrate and fat diet.

2. Several leading clinicians recommend protein milk as the diet of choice, and advocate three stages in the dietary treatment: (1) protein milk exclusively; (2) protein milk with additional protein foods; (3) protein foods with additional carbohydrate (starches, green vegetables and sugars).

3. Excellent results have been obtained in six consecutive patients, with powdered protein milk as the essential diet for many months.

4. A simple, three phased high protein diet is offered, which can be used readily in the home.

5. The tolerance for carbohydrates increases if Phases 1 and 2 are rigidly adhered to sufficiently long; exacerbations during Phase 3 necessitate the immediate omission of carbohydrates and fats and search for possible parenteral disease.

ACUTE SEROUS ENCEPHALITIS

A NEWLY RECOGNIZED DISEASE OF CHILDREN *

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In the summer of 1923, one of us (Brown), working at the Children's Hospital in Boston, observed six cases of a rapidly fatal disease in children, attended by symptoms referable to the central nervous system. In five of the cases necropsy was performed and revealed intense edema and congestion of the brain. In the summer of 1924, Symmers, working independently at Bellevue Hospital, observed five cases presenting clinical and anatomic changes identical with those encountered in Boston. Interestingly enough, four of the Boston patients were admitted to the hospital in the month of July, within a period of nine days; the remaining case was observed in the month of October. Three of the Bellevue patients entered the hospital within a period of thirty-six hours, at a time when the heat was intense and, for a while, the suspicion was entertained that there was some connection between the external temperature and the disease in question. In all of the Boston cases, however, and in two of those from Bellevue, there was no traceable relationship between the disease and prevailing climatic conditions, so that the conception of the process as a manifestation of heat stroke was not tenable, nor was there anything to suggest poisoning. On the contrary, our investigations lead us to believe that it is a form of infection, and that it presents clinically and pathologically a picture which, so far as we can learn, has not hitherto been recognized and described.

A summary of the clinical details follows. The naked eye and histologic changes in the brain in all of the patients were monotonously alike and, rather than indulge in needless repetition, they have been reserved for a later paragraph and described as a composite.

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* Received for publication, Dec. 15, 1924.

* From the Pathological Laboratories of the Harvard Medical School and Children's Hospital, Boston, and of Bellevue Hospital, New York.

THE BOSTON SERIES

CASE 1.—(Case M. M. in Reference 1.) The patient was a girl, aged 2 years and 9 months, who entered the hospital July 17, 1923. The past history was negative except for pneumonia at the age of 17 months and measles and mumps in March, 1923. The child was said to have had frequent colds and to have coughed a great deal. Five days before admission to the hospital, she began to vomit after eating or drinking, and was seen to place her hands to the head as if suffering from headache. Her temperature was 105.5 F. During the forty-eight hours that the child was in the hospital, she had several generalized convulsions and there was internal strabismus. Eyeground examination revealed distinct blurring of both discs and a small hemorrhage on the temporal side of the right. The cerebrospinal fluid was removed under apparently normal pressure and was clear; there was a moderate amount of globulin and a normal amount of sugar; the cell count on two occasions was 15 and 30; 80 and 40 per cent. polymorphonuclears; 15 and 54 per cent. small mononuclears and 5 and 6 per cent. large mononuclears.

CASE 2.—(Case J. L. in Reference 1.) The patient was a boy, aged 3½ years, who entered the hospital July 17, 1923. The past history was negative except that the child was said to have been subject to sore throat. He was well up to four days before admission, at which time he became irritable and "talked out of the side of his mouth." The mouth was drawn to the right and he had difficulty in opening the right eye. Two days before admission he became fretful, ate little and complained of sore throat. One day before admission, the patient seemed to be unable to open his mouth and developed mild diarrhea with from three to four loose brownish stools. The child's mother attempted to examine his throat, but he was seized with a convulsion, lasting for about three minutes. A physician who examined him at the time said that the nerves of the face were paralyzed. The child was put to bed, and his mother noticed that his head seemed to be drawn back and that he lay persistently on the right side; he vomited several times and complained of headache. Physical examination revealed a temperature of 103 F.; the pupils were unequal and nystagmus was present; the jaw was locked and the neck rigid; the tonsils were enlarged, inflamed and ragged. Eyeground examination revealed distinct blurring of both discs, also small hemorrhages on the temporal side of the left disc. The patient entered the hospital in a comatose condition and died a few hours later. The cerebrospinal fluid was obtained under slightly increased pressure and was clear; it contained a faint trace of globulin and a normal amount of sugar; cell count 2, both being small mononuclears.

CASE 3.—(Case H. C. in Reference 1.) The patient was a girl, aged 22 months, who entered the hospital July 21, 1923. The past history was irrelevant. About ten days before admission, while teething, the patient vomited and refused to eat, and vomited occasionally on each day thereafter. During the four days before admission to the hospital, the patient vomited everything taken. On the day of admission, she developed convulsions, each of which lasted for about five minutes. The patient died a few hours after admission to the hospital, having had eight or nine convulsions and a temperature as high as 106 F. Physical examination revealed divergent strabismus; the pupils were unequal; there was slight stiffness of the neck; tache cérébrale; the kneejerks were diminished; Kernig's sign was positive; a double Babinski sign was constant. Eyeground examination revealed distinct blurring of the margins of both discs, with two small hemorrhages in the lower medial surface on the right. The cerebrospinal fluid was removed under increased pressure; cell count from 33 to 97; slight trace of globulin and slightly increased sugar. On one occasion the differential count revealed 70 per cent. of large mononuclear cells and 30 per cent. small mononuclears; on another occasion, 15 per cent. polymorphonuclear neutrophils, 60 per cent. large mononuclear cells and 25 per cent. small mononuclear cells.

CASE 4.—(Case J. T. in Reference 1.) The patient was a boy, aged 22 months, who entered the hospital, July 26, 1923, and who had been perfectly well until November, 1922, when he developed pertussis; the cough continued until May, 1923. In April, 1923, the child had a mild attack of measles, since which time, however, he had not been doing well. His appetite was not only poor but perverted, the child chewing wood all the while. He had several attacks of vomiting and for the previous three weeks had been irritable, crying on the slightest provocation. Five days before admission to the hospital he became semistuporous with increased vomiting and remained in that state until the time of admission. Physical examination revealed a well nourished, fairly well developed, pale, listless child. Respiration was irregular, frequently sighing in character. The fundi showed marked papillo-edema of both discs, especially well marked on the left; there were no other symptoms referable to the central nervous system, with the exception of generalized convulsions which lasted for four or five hours. The temperature ranged from 100.8 to 104 F. Eight hours after admission to the hospital the child died. At the time of admission, lumbar puncture was done and 30 c.c. of clear fluid was obtained under increased pressure. The fluid was slightly yellow and contained 170 cells, 80 per cent. of which were small mononuclear cells, 8 per cent. large mononuclear cells, 4 per cent. polymorphonuclear neutrophils and 8 per cent. red cells. The cerebrospinal fluid was positive for globulin; the sugar content was 67 mg. per hundred cubic centimeters; culture was sterile.

CASE 5.—The patient was a girl, aged 4 years and 9 months, who entered the hospital Oct. 20, 1923. It was said that the patient had been apparently in perfect health until 7 a. m. the day of admission, when it was found that the left arm flexed rigidly and that the eyes were staring and rolling. At 10 a. m. she had a generalized convulsion which lasted for five minutes. At 6 p. m. she was markedly feverish and vomited twice. At the time of admission the patient was unconscious. Physical examination showed marked edema of the discs and engorgement of the retinal veins; there was marked resistance to opening the mouth; the kneejerks could not be obtained; there was left ankle clonus and a bilateral Babinski sign; no tendon reflexes were obtained in the arms except a right sided wrist jerk; abdominal reflexes were lost. Respiration was irregular, rapid and deep. During the twenty-four hours that the patient was in the hospital, she had several convulsions with steadily rising temperature which finally reached 108 F. During the convulsions the hands assumed a "main en griffe" position. The patient died the day after admission. The cerebrospinal fluid escaped under reduced pressure, only three or four drops being obtained.

Fresh material from the brain of four of these patients was injected into rabbits, both by the intracranial and corneal scratch method; material from Case 5 was injected intracranially into a monkey. The results were uniformly negative. Cultures made from the patients' cerebrospinal fluid at the time of necropsy were likewise negative, and sections of brain tissue stained by Wolbach's modification of the Giemsa method failed to show bacteria.

THE NEW YORK CASES

CASE 1.—The patient, a boy, aged 3 years, was admitted to the hospital at 11 p. m. and died two hours later. Previous to admission it is said that the child had been ill for a period of twelve hours, during which he vomited frequently and suffered from diarrhea. Four hours before admission to the hospital he was seized by generalized convulsions, which continued during the time he was under observation. The patient was comatose on admission and the right arm and leg and the right side of the face were involved in tonic spasms. The eyes were deviated to the right; kneejerks were not obtainable; the conjunctivae and pharynx were slightly reddened.

CASE 2.—The patient was a boy, aged 2 years, who was admitted to the hospital at 8 p. m. and died three hours later. At the time of admission, the patient was mentally clear; kneejerks were active; the pharynx and tonsils were injected. Respiration was shallow and rapid, at times sighing. Two hours after admission the patient developed generalized convulsions and lapsed into coma. At the time of admission the temperature was 104 F. Spinal tap revealed clear, colorless fluid which came out under increased pressure; it contained a small amount of albumin, but no globulin; it was estimated that there were about 10 lymphocytes per cubic millimeter.

CASE 3.—The patient was a boy, aged 7 years, who was said to have been perfectly well until four hours before admission to the hospital, when he was seized by a convulsion, attended by locking of the jaws, which lasted for about ten minutes. Immediately thereafter it was noted that the child was unable to move the left arm and leg. During the course of this illness the child had seven convulsions of a similar nature and was semistuporous. Physical examination revealed marked flaccidity of the left upper and lower extremities, absence of the cremasteric reflex on the left side, absent kneejerks, a positive Babinski sign on the left, and a positive Brudzinski sign on the right. There was external strabismus of the right eye; the pupils were dilated, the left being slightly larger than the right. There was slight left facial paralysis. The temperature was 102 F. on admission and rose to 106 on the second day. The cerebrospinal fluid was clear and came out under apparently normal pressure; sugar and albumin + +; cells 9.

CASE 4.—The patient, a girl, aged 2 years, died immediately after admission to the hospital. Little could be learned of her except that she had had repeated convulsions over a period of about fifteen hours, and that for two weeks previous to her death she had been irritable and had suffered from attacks of vomiting and diarrhea.

CASE 5.—The patient was a girl, aged 14 months. Her mother stated that the day before admission to the hospital the child had passed 6 large green stools and suddenly became listless. At the time of admission, the child was somewhat stuporous, but otherwise presented nothing worthy of note in the present connection. There were no localizing symptoms referable to derangement of the central nervous system. On the fifth day after admission, the child's temperature was 105 F., and she had frequent convulsions throughout the day. The convulsions were generalized, starting in the right arm, and continued in spite of the use of bromid and chloral. Respiration was rapid, sometimes crowing. The cerebrospinal fluid was clear and was obtained under slightly increased pressure; there was no albumin or globulin; there were 150 cells, most of them lymphocytes. The child died at noon on the fifth day after admission to the hospital.

COMMENT

This series includes ten cases of a fatal disease encountered in children. The youngest child was 22 months of age, the oldest 7 years, the average age being slightly less than 28 months. The disease occurred five times in females and five times in males. The condition is of rapid onset and is initiated by such symptoms as irritability, lack of appetite, vomiting or diarrhea or both, and noticeably often by sore throat, the whole followed by elevation of temperature, sometimes to the extent of 105 or 106 F. and by signs referable to derangement of the central nervous system, among them bulbar signs in the form of respiratory irregularities, ptosis, strabismus, nystagmus, papilledema, retraction of

the angle of the mouth, muscular twitchings, rigidity of the neck or jaw, hemiplegia, coma, convulsions and death within thirty-six or forty-eight hours or, at longest, a few days. The cases are separable into two clinical groups, one in which convulsions are associated with one or several of the localizing signs which have just been enumerated; in the second group no such signs are present and the only obvious symptom of derangement of the central nervous system is to be found in the convulsions. The most striking feature of the convulsions is that they are

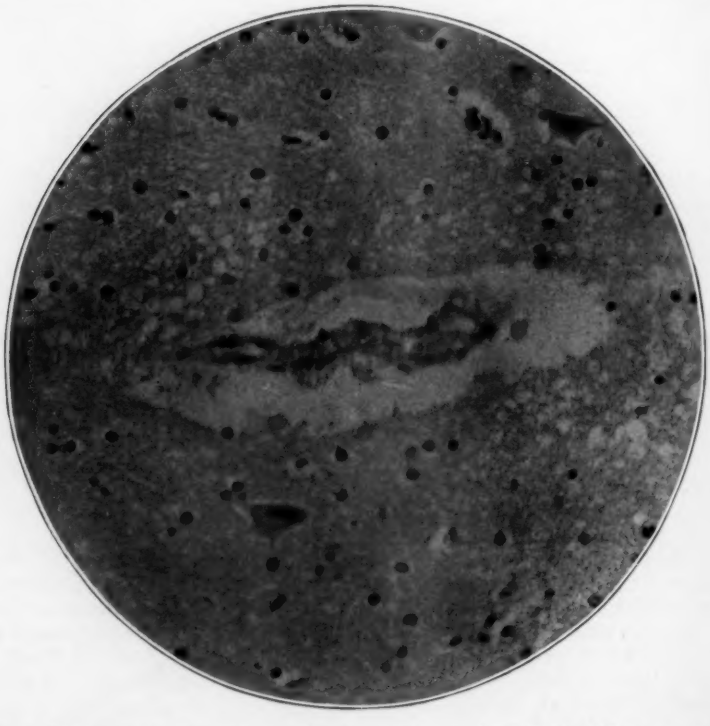

Fig. 1.—Edema in caudate nucleus, mostly perivascular (Case 3, Boston Series).

absolutely uncontrollable by any of the measures commonly employed for this purpose, including the use of such drugs as morphin and chloral.

Anatomically, the disease is characterized by extreme enlargement of the brain, so much so that the brain bulges when the dura is opened. The pia-arachnoid presents an intense degree of engorgement, and splotch-like hemorrhages may be present. The convolutions are flattened to an extraordinary extent, the sulci are obliterated, and the brain is so soft as to give one the sensation of flowing. On section, the substance of the brain is pinkish.

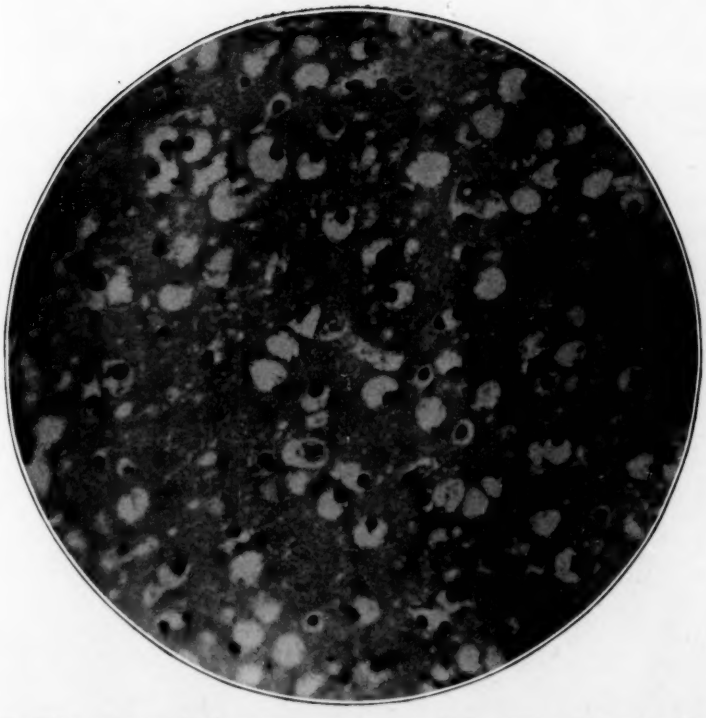

Fig. 2.—Edema in cerebral cortex, mostly pericellular (Case 3, Boston Series).

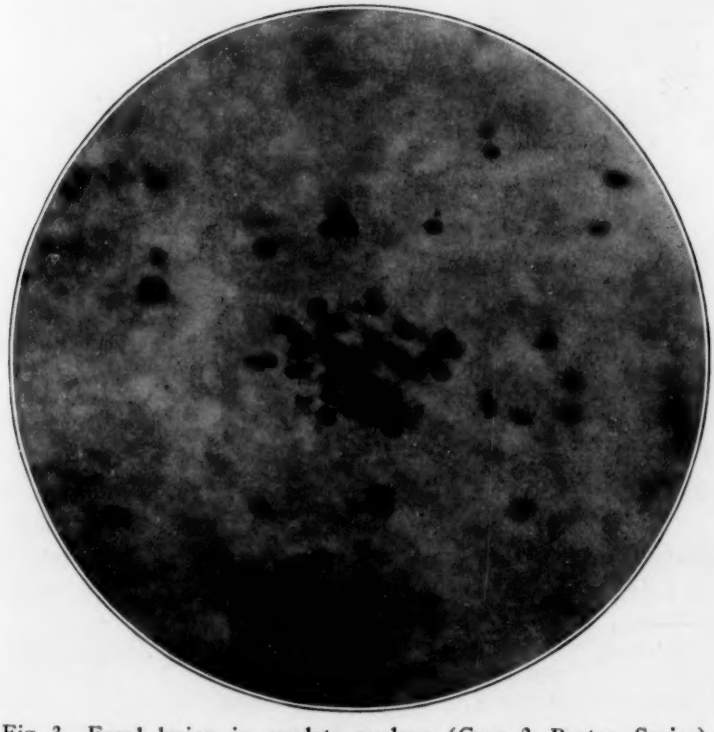

Fig. 3.—Focal lesion in caudate nucleus (Case 3, Boston Series).

Microscopically, the most constant changes are to be found in hyperemia and edema of the pia-arachnoid, engorgement of the blood vessels of the brain, perivascular and pericellular edema, with or without vacuolation of the ground substance, and acute cloudy swelling of the pyramidal cells. Every capillary in the brain is crowded with red blood corpuscles, almost to the point of bursting.[1] Hemorrhages into the brain, however, are conspicuous by their rarity. Practically every one of the blood vessels is surrounded by an apparently empty space, corresponding

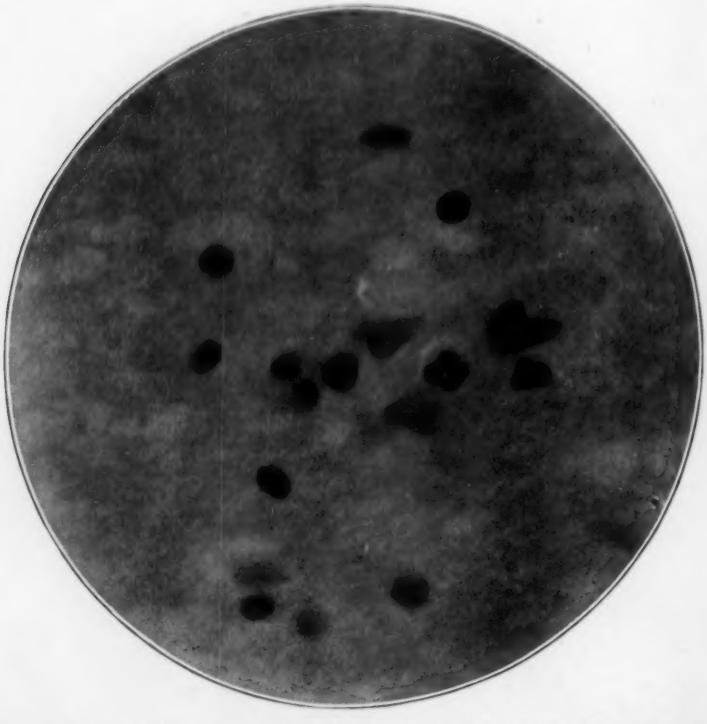

Fig. 4.—Focal lesion in cerebral cortex. One polymorphonuclear leukocyte is seen in focus (Case 3, Boston Series).

to an area of edema (Fig. 1). In places, the microscopic picture is marked by the presence of numerous glia cells, each of which lies in what appears to be a vacuole, but which again represents an area of edema (Fig. 2). In some cases there are focal collections of a dozen[2] or more cells made up of glia cells, together with cells of the lymphocytic type and occasionally a polymorphonuclear neutrophil (Figs. 3 and 4).

1. Anderson, Arthur F.: Report of Five Cases of Acute Encephalitis, Boston M. & S. J. **189**:177 (Aug. 2) 1923 .

2. Editorial: Boston M. & S. J. **189**:256 (Aug. 16) 1923.

In still other instances, small collections of cells of the purely lymphocytic type are encountered. Such foci, while not constant, are to be seen with sufficient frequency to merit consideration. Occasionally the wall of an arteriole is more cellular than in ordinary circumstances due, apparently, to proliferation of endothelial cells. In none of our microscopic preparations, including practically every part of the brain, have we in a single instance encountered the cellular infiltration which is so characteristic of poliomyelitis and epidemic encephalitis. On the other hand, the intense injection of blood vessels and the presence of clear spaces around vessels and cells, corresponding to areas of edema, suggest that we are dealing with a vascular disease attended by the escape of serum rather than cells; that is to say, that the disease belongs in the same general category with the so-called encephalitis lethargica. Or it is possible that the intense edema and congestion of the brain are secondary phenomena, representing the mechanical effects of repeated convulsive seizures which, however, is contrary to the experience of pathologists. If this be the case, the condition obviously does not warrant the descriptive title of serous encephalitis. However inapt the designation may be, the fact remains that the disease challenges attention both from the standpoint of recognition at the bedside and further inquiry into its nature and cause.

RAT-BITE FEVER

A CLINICAL REVIEW WITH REPORT OF A CASE *

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AND
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The clinical entity known as rat-bite fever, and first described in this country by Wilcox [1] in 1840, presents an interesting group of symptoms, and, while it cannot be classed as a rarity, is, however, of comparatively infrequent occurrence in America. Most of the cases described have occurred in adults, with very little, if any, variability in symptoms. The case reported here, in an infant, aged 7 months, is, therefore, of further interest, particularly from the standpoint of the pediatrician.

REPORT OF CASE

M. De R., a girl, aged 7 months, was brought to the outpatient dispensary, Aug. 4, 1924, suffering from severe diarrhea and vomiting. She refused all food and seemed quite ill, the symptoms having persisted for four days previous to admission. Five days previously she had been bitten on the left hand by a rat. When admitted to hospital, the stools were green and watery, and the child vomited everything taken by mouth.

The family and past histories were not remarkable.

Physical Examination.—The child appeared acutely ill and was badly dehydrated. The skin was pale and of an icteric tint. The head presented no abnormalities. Both fontanels were open and there was no pulsation or bulging. The eyes were normal. The mouth showed nothing abnormal; there were no teeth. A few cervical glands were palpable on the left side. The heart and lungs were negative. The skin of the abdomen was dry and wrinkled; the liver and spleen were not enlarged. There were no visible peristaltic waves. The left hand showed two small scars on the thenar eminence, but there was no swelling or redness. The reflexes showed nothing abnormal. In the left axilla an enlarged gland could be palpated. The temperature on admission was 38.4 C. (101.1 F.).

Clinical Course.—The day following admission the child was given 400 c.c. of physiologic sodium chlorid solution by the intraperitoneal route. A small amount of water and casein given by mouth was retained. On the nineteenth day following the rat bite, the left hand became swollen in the region of the bite scars, accompanied by a dusky induration. The skin over this area was tense. The temperature was 38 C. (100.2 F.) and the child was extremely irritable. She took very little food by mouth and was accordingly given an additional 300 c.c. of saline solution by way of the peritoneum. The next day the condition was practically unchanged. The swelling had increased, the temperature was high, and in addition there was marked hyperesthesia. Slight

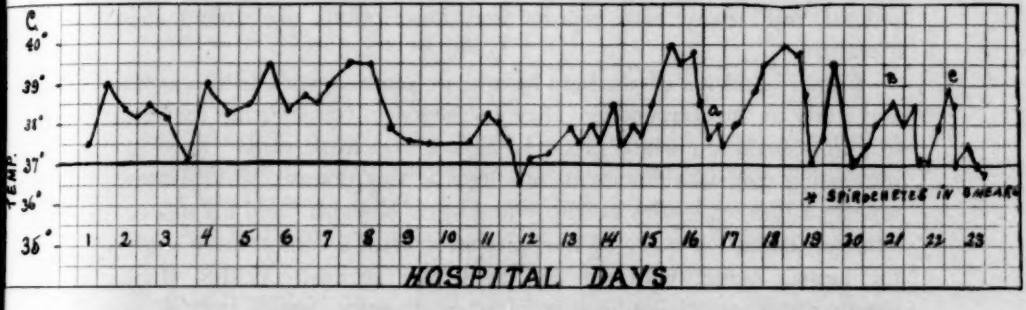
* Received for publication, Nov. 7, 1924.

* From the Pediatric Service of St. Luke's Hospital.

1. Wilcox, W.: Am. J. M. Sc. **26**:245, 1840.

jarring of the bed or the slightest manipulation elicited sharp cries. The anterior fontanel was tense and pulsating and there was definite neck rigidity. Kernig's sign was questionable. The lungs were clear and the ears normal. Meningitis was considered at this time and the child isolated. Hot compresses were applied continuously to the affected hand, with little improvement. On surgical consultation, an incision was advised. No pus was obtained, and the swelling and discoloration became more marked. A slight purplish, macular eruption was seen at this time in the region of the swelling. It was not observed elsewhere on the body. A dark-field examination of serum taken from the wound revealed no spirochetes. There were definite remissions of fever. Three days later a second examination of serum (under dark-field illumination) by Dr. Thayer showed several spirochetes. We are indebted to Dr. Thayer for the following report.

The ball of the thumb was very edematous and marked by two small wounds at opposite sides of the part, which were partly cicatrized, dry and with no discharge. A sterile needle was introduced deep into the wound on the palmar aspect about half across the swollen part, and one or two drops of lymph removed. These were placed on clean slides, mixed with a drop of sterile salt solution (0.95 per cent.) and examined by dark-field illumination. A small spirochetal organism not over 5 microns in length, more sluggish in



Temperature curve showing characteristic paroxysms and effect of sulpharsphenamin injections. A=0.05 gm. sulpharsphenamin, B=0.05 gm. sulpharsphenamin, C=0.05 gm. sulpharsphenamin.

movement than the *Spirochaeta pallida,* showing a screwlike twisting and a lateral swaying, but no intrinsic wave along the course of the organism itself was observed in each specimen. The numbers of these organisms could not be estimated exactly, but they were relatively scarce in each slide. Following this report, 0.05 gm. of sulpharsphenamin was injected intramuscularly. At the time of injection the temperature was 37.6 C. (99.4 F.). The condition of the hand remained unchanged and the axillary nodes on the left side were enlarged and tender. The next day the temperature rose to 38 C. (100.2 F.). Two days later the same dose of sulpharsphenamin was repeated, followed by a third injection in two days. The hand at this time was completely healed, and the child's general condition showed a marked improvement. Nourishment was taken and retained and the skin turgor was better.

During the week following the patient improved rapidly. There was a slight gain in weight and she seemed much brighter. In the interval there had been several paroxysms of fever. During convalescence she developed a cough which later became paroxysmal, and a diagnosis of pertussis was made. She was transferred to the contagious division of the City Hospital. A subsequent report stated that her general condition had improved greatly.

Laboratory Findings.—Urinalysis was negative. Blood examination, August 16, showed hemoglobin, 85 per cent., 4,521,000 red blood cells and 12,000 leukocytes. The differential count revealed 62 per cent. polymorphonuclears and 31 per cent. lymphocytes. There was some anisocytosis and poikilocytosis. August 20, the hemoglobin had dropped to 50 per cent. and the leukocytes had risen to 20,400. August 22, the red cells numbered 2,272,000, with a hemoglobin of 40 per cent. The blood Wassermann was negative.

Treatment.—Except for three injections of sulpharsphenamin, this was largely symptomatic. Bismuth and paregoric were given to control diarrhea, plus casein and water by mouth, with intraperitoneal injections of saline solution when indicated.

The case just described is essentially typical, differing only in the distribution and intensity of the rash. Hyperesthesia was a well marked feature, reminding one of that symptom in acute poliomyelitis.

REVIEW OF THE LITERATURE

In reviewing the literature we note that the Japanese investigators have carried on intensive research, particularly in regard to the etiology, and are responsible for the discovery of the causative factor, the *Spirochaeta morsus-muris*. The disease in that country is known as sodoku, and many case reports and descriptions are found in the literature.

Futaki [2] and his co-workers have done pioneer work in the isolation and study of the spirochete. They succeeded in transmitting the disease to guinea-pigs and white rats. Kitagawa and Mukoyama [3] have made interesting contributions on the etiology of this disease, while Kaneko [4] reports a fatal case with necropsy findings. Kusama [5] and his associates made an extensive study of the spirochete, with a comparative study of the human being, wild rat and field vole strains. Within the last twenty years cases have been reported in America, Spain, Italy, France, England, Germany and Australia. Low [6] reports a case in England with recovery of the spirochete from the blood. Spaar [7] cites two cases in which the organism was not found. In Solly's [8] case no spirochetes were found, although the clinical course was typical. Cumston [9] dis-

2. Futaki, K.; Takaki, F.; Taniguchi, T., and Osumi, S.: The Cause of Rat-Bite Fever, J. Exper. Med. **23**:249 (Feb.) 1916.

3. Kitagawa, J., and Mukoyama, T.: The Etiologic Agent of Rat-Bite Disease, Arch. Int. Med. **20**:317 (Sept.) 1917.

4. Kaneko, R.: Contribution to the Etiology and Pathology of Rat-Bite Fever, J. Exper. Med. **26**:363 (Sept.) 1917.

5. Kusama, S.; Kobayashi, R., and Kasai, K.: The Rat-Bite Fever Spirochete, with Comparative Study of Human, Wild Rat and Field Vole Strains, J. Infect. Dis. **24**:366 (April) 1919.

6. Low, G. C.: A Case of Rat-Bite Fever in England, Recovery of the Spirochete from the Blood, Brit. M. J. **1**:236 (Feb. 9) 1924.

7. Spaar, E. C.: Two Cases of Rat-Bite Fever; Rapid Cure by Intravenous Injection of Neosalvarsan, J. Trop. Med. **26**:239-243 (July 16) 1923.

8. Solly, R. V.: Rat-bite Fever, Lancet **1**:458 (March 22) 1919.

9. Cumston, C. G.: Sodoku or Rat-Bite Fever, New York M. J. **110**:197 (Aug. 2) 1919.

cusses the symptomatology, and states that many cases occurred among the soldiers during the recent war. Mooser [10] reports two cases in which he was unable to isolate the spirochete. Paramand [11] cites several cases in India. He isolated the spirochete from one case and from three inoculated animals (guinea-pigs and white rats). Nixon's [12] case was caused by the bite of a ferret. Ruggiero,[13] Cazamian,[14] and Troisier [15] report cases in Italy and France. One of the best articles in the American literature is that by Crohn.[16] He reviews the cases reported from various countries and adds several of his own. The most recent case reports are those of Strauch and Bissell [17] and Reuben and Steffen.[18]

DEFINITION

Rat-bite fever may be defined as an infectious disease caused usually by the bite of a rat, and characterized by paroxysms of fever (remittent or intermittent), an inflammatory reaction at the site of the wound, enlargement and tenderness of the adjacent lymph glands, and by a more or less characteristic exanthem. Less commonly the condition follows the bite of a ferret, cat, dog or squirrel.

ETIOLOGY

The disease is not common in this country. Frequent occurrence is most notable in Japan, owing, probably, to the housing conditions. Age and sex have no influence. Regarding the exciting factor, it has been shown that the *Spirochaeta morsus-muris* is in all probability the the organism responsible for the characteristic syndrome.

This is described as a short, thick spirochete with tapered ends, ranging in size from 2 to 12 microns. The curves vary from two or three to six. Several modifications have been described, one type showing a short, thick body while the other is long and thin. The tapered ends often take the form of flagella. The spirochete stains readily with

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10. Mooser, H.: Experimental Studies with a Spiral Organism Found in a Wild Rat, J. Exper. Med. **39**:589 (April) 1924.

11. Paramand, M. J.: Rate-Bite Fever with Special Reference to Its Etiologic Agent, Indian J. M. Res. **11**:181-185, 1923-1924.

12. Nixon, J. H.: Rat-Bite Fever Caused by a Ferret, Brit. M. J. **2**:629, 1914.

13. Ruggiero, A.: Rat-Bite Fever in Woman, Policlinico **29**:781-786 (June 12) 1922.

14. Cazamian, P.: Rat-Bite Fever from a Dog Bite, Bull. et mém. Soc. méd. d. hôp. de Paris **45**:268 (Feb. 25) 1921.

15. Troisier, J., and Clément, R.: A Case of Rat-Bite Fever at Paris, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:542-549 (March 21) 1922.

16. Crohn, B. B.: Rat-Bite Fever, Arch. Int. Med. **15**:1014 (June) 1915.

17. Strauch, A., and Bissell, B. G.: Rat-Bite Fever, Arch. Pediat. **41**:315 (May) 1924.

18. Reuben, M. S., and Steffen, W. C.: Rat-Bite Fever, Arch. Pediat. **41**:499 (July) 1924.

Leischman's and Giemsa's preparations, also with dilute carbolfuchsin. According to Kusama and his co-workers, with Fontana's method of silver impregnation staining, the spirochete swells up and assumes a spindle-like appearance with the curves barely visible. It can also be demonstrated by dark-field illumination and by Burri's India ink method.

Regarding the distribution of the organism, it has been found in the skin areas showing the eruption, in the glands, in the bite wound, and in the blood during the paroxysms of fever. It is rarely excreted in the urine. Kusama found a generalized distribution in infected rats and guinea-pigs after two weeks. This includes the subcutaneous and submucous tissues of the eyelids, lips and tongue; the capsules of the salivary and lymph glands; the heart wall and the adventitia of the aorta and the large arteries within the visceral organs; the spleen, liver, kidneys and suprarenals and sometimes in the endocardium. The organism is doubtless transmitted through the saliva of the infected animal.

Other organisms have been advanced as the etiologic factor. Schottmüller [19] isolated a streptothrix in eight consecutive blood cultures from his case. This he designated the *Streptothrix muris-ratti*. Blake [20] confirmed his findings, while Tileston [21] recovered under dark-field examination a similar organism. Blake's case showed an ulcerative endocarditis, the streptothrix being recovered from the mitral valve. In Proescher's [22] case, a number of bacilli were isolated which stained a bluish color with Giemsa solution. These were found singly and in pairs. In our case a spirochete was found corresponding morphologically with that described by the Japanese observers. Opinions vary as to the exact organism producing the disease. However, the influence of arsphenamin and the allied arsenical preparations on the course of the disease is, we believe, strong evidence in favor of a spirochetal infection as the underlying cause.

PATHOLOGY

Comparatively little is known concerning the pathologic changes in this disease. In Blake's case the chief findings included an ulcerative endocarditis, passive congestion of the lungs and liver, and two areas of splenic infarction. Histologically, the heart showed a cellular infiltration, while sections of the liver and kidneys revealed a subacute inter-

19. Schottmüller, H.: Dermat. Wchnschr. **58**: Supplement 77, 1914.
20. Blake, F. G.: The Etiology of Rat-Bite Fever, J. Exper. Med. **23**:39 (Jan.) 1916.
21. Tileston, Wilder: The Etiology and Treatment of Rat-Bite Fever, J. A. M. A. **66**:995 (April) 1916.
22. Proescher, F.: Rat-Bite Disease, with Report of a New Case, Internat. Clin., Series 21, **4**:47, 1911.

stitial hepatitis and glomerular and interstitial nephritis. There was also some perivascular exudation in the suprarenals. In Miura's [23] case there was marked increase of the cerebrospinal fluid, with hyperemia of the pia mater and spinal cord. Several fatal cases reported by other authors, in which necropsies were performed, gave nothing definite regarding pathology which could be attributed to rat-bite fever per se. The patients were advanced in years (from 68 and 70 years), and the findings consisted chiefly of the sclerotic changes common to persons of these ages.

CLINICAL TYPES

Writers differ as to their classification. Crohn mentions four classes: (1) the afebrile, mild in character; (2) the febrile, characterized by continued fever, marked nervous symptoms, and fatal termination; or, pursuing a mild course with slight systemic reaction; (3) the intermittent type, with recurrent pyrexial attacks and a local inflammatory reaction with a bluish-red exanthem; and (4) miscellaneous types showing differences in the clinical course.

Miyake [24] divides the disease into three types: (1) the febrile form; (2) the afebrile forms with predominating nervous symptoms, and (3) the abortive form. The afebrile forms are further subdivided into the acute and subacute cases. In the former the course is rapid and accompanied by severe pain at the seat of the bite, asthenia, vertigo, dyspnea, headache, small pulse, delirium, sensory and motor paralysis, and collapse, usually with fatal termination. The exanthem is not always observed. The subacute form has a longer incubation period and persists over a period of a few months or longer.

INCUBATION

The period of incubation is usually from ten to twenty-eight days, with an average of two weeks. Longer periods have been reported, up to one year or more, but these are open to question.

PRODROMES

Most of the cases show no prodromal symptoms. When occurring they consist of vague muscular pains, headache, malaise and weakness.

SYMPTOMATOLOGY

The disease is usually ushered in by simultaneous local and systemic reactions. The healed area of the bite becomes painful, swollen, and of a red-blue color. The adjacent lymphatic glands become enlarged and

23. Quoted by Proescher, footnote 22.
24. Quoted by Proescher, footnote 22.

tender. The wound, as a rule, does not suppurate, although the local manifestations often suggest the presence of pus. The edema resembles that seen in nephritis.

Coincident with the local reaction are fever (from 102 to 105 F.), chilly sensations or actual rigors, muscle pains and tenderness, asthenia, headache, and joint pains. Nausea and vomiting may be present, and in severe cases delirium and stupor. The fever continues high for several days, declining by crisis, less often by lysis. This is followed by an abatement of symptoms with marked diaphoresis. A period of apyrexia then intervenes, lasting from two to six days, and followed by a second rise in temperature with its concomitant symptoms. This cycle is repeated over a variable period, the duration depending on the severity of the infection and the character of the treatment instituted. The remissions may extend over a period of weeks or months or even longer. In Surveyor's [25] case the febrile paroxysms continued intermittently for eight years.

The rash appears usually during the first few paroxysms, and is characterized by bluish-red macules with well-defined margins, varying from 1 to 9 mm. in diameter. The distribution is either local or general. O'Leary,[26] who studied particularly the dermatologic aspects of this disease, states that the exanthematic phase of rat-bite fever may be classified under the groups of roseola, indurated erythematous plaques, urticarial manifestations, lesions of the mucous membranes and alopecia. One of his patients developed patches of erythema on the face and later on the lower extremities, intensified during the exacerbations of fever. The skin cleared under arsphenamin therapy.

If the disease runs a protracted course, emaciation and cachexia become prominent features, accompanied by marked nervous symptoms. Hyperesthesia, paresthesia or anesthesia are common. In some cases there is a paralysis of the lower extremities. The wound in most cases shows only a moderately severe inflammatory reaction. Occasionally there is a circumscribed area of necrosis.

PHYSICAL FINDINGS

These include the skin eruption, the local inflammation at the bite area and glandular enlargement. In addition, the heart may reveal a hemic murmur, while the lungs sometimes show signs of bronchitis. The liver and spleen are not enlarged. The patellar and tendon reflexes may be exaggerated.

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25. Surveyor, N. F.: A Case of Rat-Bite Fever Treated with Neosalvarsan, Lancet **2**:1764, 1913.

26. O'Leary, Paul A.: The Dermatologic Aspects of Rat-Bite Fever, Arch. Dermat. & Syph. **9**:293 (March) 1924.

THE BLOOD

Leukocytosis is a prominent feature, ranging from twelve to twenty thousand. The polymorphonuclear neutrophils are relatively increased, and a slight eosinophilia is not uncommon. During the periods of apyrexia the count may be lower. The blood Wassermann test may or may not be positive. A positive reaction carries no great significance therefore, from the standpoint of a coexistent syphilitic infection, since it may be found positive in any spirochetal disease. The hemoglobin and red cells are reduced, secondary anemia progressing with the disease.

THE URINE

Toxic nephritis, mild or severe, sometimes occurs. The urine then shows large amounts of albumin and many hyaline and granular casts. Ordinarily, the findings are simply those of any febrile disease: a concentrated urine with slight or moderate amounts of albumin.

DIAGNOSIS

The diagnosis as a rule is not difficult. Obviously, the first point is a positive history of a bite, either from the rat or one of the other animals mentioned. With the onset of the clinical features four cardinal symptoms are noted: intermittent or remittent fever; a characteristic bluish-red exanthem; muscular pains and tenderness and a local inflammation at the bite area. Other symptoms may be associated, but these occupy the foreground.

Regarding the differential diagnosis, several conditions must be considered, notably malaria, septicemia, erysipelas and relapsing fever. Malaria can easily be differentiated by finding the parasite in the blood and by enlargement of the liver and spleen. From erysipelas it may be differentiated by absence of a sharply demarcated, dusky, indurated inflammatory area with vesiculation, and the continued fever during the active stages of the disease. Septicemia is characterized by septic fever remissions, the presence of the exciting organism in the blood, metastatic abscesses and a petechial or vesicular eruption. Relapsing fever shows the presence in the blood of the characteristic spirochete, infection taking place through the bite of a louse. The systemic reaction is marked, epistaxis is common, and hemorrhage into the skin and in the gastrointestinal tract is frequent.

COMPLICATIONS AND SEQUELAE

The chief complication is nephritis. Sequelae such as general weakness and pains in various parts of the body are not uncommon.

PROGNOSIS

The prognosis in ordinary, uncomplicated cases is usually good. It depends largely on the severity of the disease, the physical make-up and resistance of the patient, and the nature of the treatment. Edema, marked nervous symptoms, continued high fever, progressive asthenia and cachexia are unfavorable signs. The fatal cases, in most instances, terminate by collapse. The mortality has been placed at 10 per cent. Since the introduction of arsphenamin as a measure of therapy, however, the mortality rate will probably be lowered.

TREATMENT

Prophylaxis is best accomplished by complete cauterization of the wound as soon as possible after the bite. Pure phenol (carbolic acid) is the best agent, and this should be supplemented by wet dressings of a mercuric chlorid solution (1:3,000). Miyake advocates the injection of a 5 per cent. phenol (carbolic acid) solution about the wound.

Arsphenamin, neo-arsphenamin or sulpharsphenamin act specifically. Many of the cases reported have cleared up after one injection, while protracted cases eventually yield to repeated injections. In our case three injections of sulpharsphenamin were sufficient to cause recovery.

Therapy along other lines is largely symptomatic. The opiates, acetylsalicylic acid or acetphenetidin-U. S. P. may be administered to relieve the muscular pains. Fever may be partially controlled by tepid sponging and the judicious use of the coal-tar products. The diet should be light and nutritious. During convalescence, bitter tonics or an iron and strychnin combination are valuable aids.

SUMMARY

1. A case of rat-bite fever in an infant, aged 7 months, is reported.

2. The clinical picture was essentially the same as that described by other authors.

3. The *Spirochaeta morsus-muris* was recovered from serum taken from the bite wound, by examination under dark-field illumination.

4. Recovery took place under sulpharsphenamin therapy, three injections, each of 0.05 gm. sufficing.

5. A review of the literature shows a comparatively small number of cases reported in this country during the last ten years.

6. The consensus of opinion is in favor of the *Spirochaeta morsus-muris* as the exciting factor.

7. Comparatively little is known concerning the pathologic changes resulting from the disease.

8. The general clinical picture is one of a moderate or severe toxemia with a characteristic temperature curve.

URIC ACID METABOLISM OF CHILDREN*

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In a previous article,[1] we reported an investigation showing the effect of various purin-free diets on the daily excretion of uric acid. The diets used were a high protein, a high fat and a high carbohydrate, which were continued over periods varying from two to four days. It was found that the high protein purin-free diet resulted in the largest excretion of uric acid in the urine. This result confirmed the reports of other investigators,[2] who have demonstrated that the ingestion of food free from purin precursors, especially the proteins, may markedly raise the level of endogenous uric acid excretion.

In discussing this fact, we stated at that time, that:

> While a high protein diet is a factor in the increased elimination of uric acid, it cannot be regarded as a quantitative one, for the protein ingestion in Case 2 was almost four times as much as that of the control diet; whereas, the uric acid excretion was only about one-tenth greater than that observed with the control diet. A possible explanation may be that a slight increase of protein is sufficient to stimulate the organism to increased purin metabolism, and that further addition of protein increases the amount of uric acid elimination up to a certain point which may be termed the limit of protein action. Beyond this, an additional intake of protein is without appreciable effect on the uric acid elimination.

The present studies were undertaken to determine the correctness of this assertion and also to study the effect on the daily uric acid excretion, of gradual increases in the protein portion of the diet.

In our previous studies, the increase from the normal to the high protein diet was effected in one step. As a result, there was no possible way of determining whether any variations occurred in the uric acid excretion following the ingestion of food containing varying amounts of protein. In the present observations, it was possible to determine this factor by gradually increasing the protein of the diet.

* Received for publication, Dec. 2, 1924.

* From the Pathological Laboratory and the A. Jacobi Division for Children, Lenox Hill Hospital.

1. Leopold, Jerome S.; Bernhard, Adolph, and Jacobi, Harry G.: Studies in the Uric Acid Metabolism of Children, Am. J. Dis. Child. **27**:243-255 (March) 1924.

2. Mares, F.: Arch. slav. Biol. **3**:207, abstr., Centralbl. f. d. med. Wissensch. **26**:2, 1888. Taylor, A. E., and Rose, W. C.: J. Biol. Chem. **18**:519, 1914. Hopkins, F. G., and Hope, W. B.: J. Physiol. **23**:271, 1898-1899. Smetanka, F.: Arch. f. d. ges. Physiol. **138**:217, 1911. Lambling, E., and Dubois, F.: Compt, rend. Soc. de biol. **76**:614, 1914. Folin, O.: Am. J. Physiol. **13**:66-117, 1905. Mendel, L. B., and Stehle, R. L.: J. Biol. Chem. **22**:215, 1915.

METABOLIC STUDIES

The studies were made on four normal children, who were kept under observation in the hospital wards. In two of the patients, the diet used at the beginning of the observation period was a normal mixed purin-free diet, while in the other two a diet consisting of several bran muffins and water was continued over a period of three days, followed by the normal mixed purin-free diet. At intervals of three or four days the protein portion of the diet was increased in each case, and the carbohydrates and fats were decreased so as not to have too high a caloric value in diet for the particular case. The total fluid intake and output for the twenty-four hour period was measured and the uric acid excretion in the urine determined. The patients were weighed daily at about the same time and chemical determinations on the blood were made on the first day of each new dietary period. During at least one day of each dietary period the urine was collected at two hourly intervals, and the uric acid content of each specimen was determined.

REPORT OF CASES

CASE 1 (Tables 1, 2 and 3, Chart 1).—A. W., aged 11 years, observed for a period of eleven days, during the first four days was given a mixed purin-free diet consisting of protein, 78.3 gm.; fat, 98.7 gm.; carbohydrate, 55.3 gm.; the twenty-four hour fluid intake and output were recorded and the uric acid

TABLE 1 *(Case 1).—Summary of Findings: Chorea*

Date	Diet			Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.
	Protein	Fat	Carbohydrates					
4/ 7*	78.3	98.7	55.3	1,466	34.2	1,400	1,365	280
4/ 8		Same		Same	34.1	1,200	1,150	265
4/ 9		Same		Same	34.1	1,200	1,100	260
4/10†		Same		Same	34.0	1,000	930	303
4/11*	99.7	65	52	1,095	34.1	1,000	950	440
4/12		Same		Same	34.0	1,000	1,005	502
4/13		Same		Same	34.1	1,000	990	536
4/14*†	120	52	64	1,238	34.2	1,000	933	420
4/15		Same		Same	34.2	900	850	400
4/16*		Same		Same	34.2	1,000	940	380
4/17		Same		Same	34.2	850	800	352

* Days on which chemical determinations on the blood were made.
† Days on which two-hour excretions of urine were collected.

excretion determined. On the first of this four-day period, chemical examinations of the blood were made. On the last day, specimens of urine were collected every two hours from 6 a. m. to 8 p. m. and a night specimen from 8 p. m. to 6 a. m. The uric acid content of these specimens was determined. For the next three days the diet consisted of protein, 99.7 gm.; fat, 65 gm.; carbohydrate, 52 gm. Chemical examinations of the blood were made on the first day. The patient was then put on a diet of protein, 120 gm.; fat, 52 gm.; carbohydrate, 64 gm. for the last four days of observation. Chemical examinations of the blood were made on the first and third days of the last period and two hourly specimens of urine collected on the first day. Each day at approximately the same time, the patient was weighed. Chart 1 shows graphically the relationship between the protein intake and the daily uric acid excretion.

TABLE 2 *(Case 1).—Chemical Determinations on the Blood*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
4/ 7	18	2.0	2.8	72
4/11	16	2.3	2.6	92
4/14	21.5	1.5	2.5	85
4/16	18	2.1	2.0	92

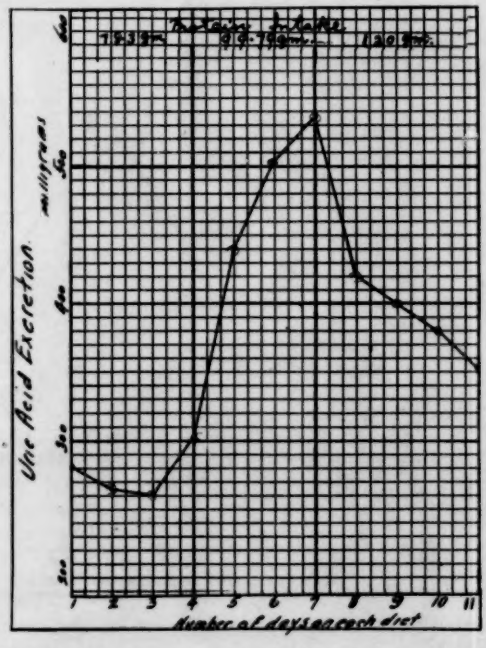

Chart 1.—Relationship between the protein intake and the daily uric acid excretion in Case 1.

TABLE 3 *(Case 1).—Two Hour Excretions of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output	Uric Acid Excretion
4/10	78.3	98.7	55.3	6 a.m. to 8 a.m.	25	19
				8 a.m. to 10 a.m.	165	26
				10 a.m. to 12 m.	40	27
				12 m. to 2 p.m.	95	37
				2 p.m. to 4 p.m.	140	46
				4 p.m. to 6 p.m.	165	50
				6 p.m. to 8 p.m.	125	38
				8 p.m. to 6 a.m.	175	60
4/14	120	52	64	6 a.m. to 8 a.m.	23	31.5
				8 a.m. to 10 a.m.	40	37
				10 a.m. to 12 m.	30	33
				12 m. to 2 p.m.	135	36
				2 p.m. to 4 p.m.	55	39.5
				4 p.m. to 6 p.m.	120	57
				6 p.m. to 8 p.m.	160	45.5
				8 p.m. to 6 a.m.	370	140.5

Case 2 (Tables 4, 5 and 6, Chart 2).—J. N., aged 10 years, was observed over a period of eleven days, the procedures being similar to those in Case 1.

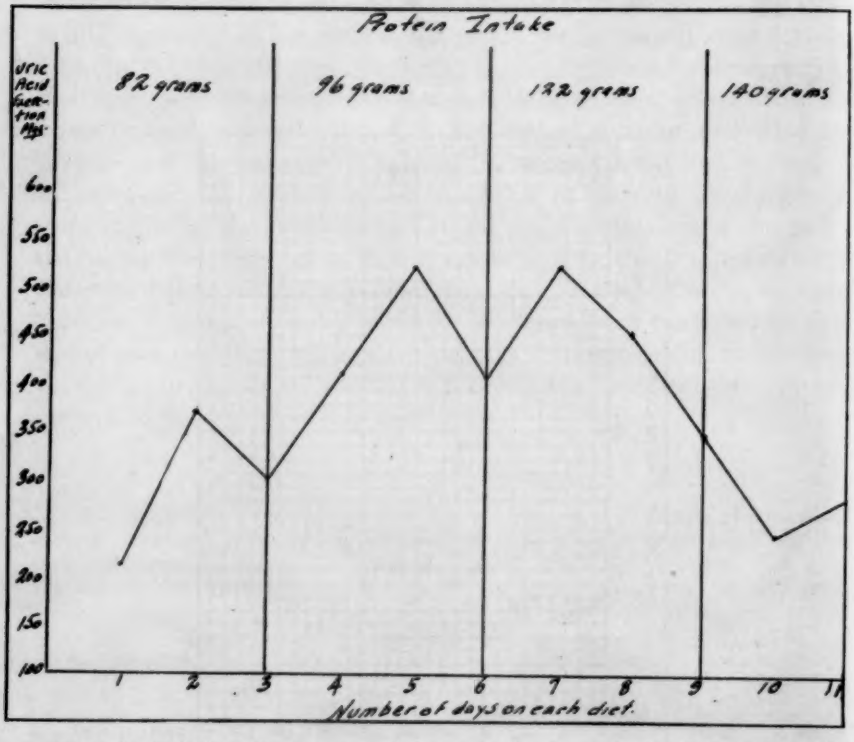

Chart 2.—Relationship between the protein intake and the daily uric acid excretion in Case 2.

Table 4 *(Case 2).—Summary of Findings: Chorea*

Date	Diet			Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.
	Protein	Fat	Carbohydrates					
4/14*	82	96	52	1,438	29.8	700	600	212
4/15		Same		Same	29.6	800	775	372
4/16†		Same		Same	29.5	800	778	301.9
4/17*	96	61	68	1,240	29.4	850	820	410
4/18		Same		Same	29.5	1,045	1,000	522
4/19†		Same		Same	29.5	950	945	408.5
4/20*	122	65	68	1,383.5	29.6	860	850	521
4/21		Same		Same	29.7	1,080	1,050	452
4/22†		Same		Same	29.7	1,000	994	347.5
4/23*	140	65	68	1,457	29.8	1,020	1,000	245
4/24		Same		Same	29.7	1,000	980	285

* Days on which chemical determinations on the blood were made.
† Days on which two-hour excretions of urine were collected.

TABLE 5 *(Case 2).—Chemical Determinations on the Blood*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
4/14	23.5	1.0	3.0	80
4/17	16.2	1.5	2.8	95
4/20	18.0	1.5	2.3	90
4/23	20.0	1.0	3.8	95

TABLE 6 *(Case 2).—Two-Hour Excretions of Uric Acid*

	Diet					
Date	Protein	Fat	Carbohydrate	Time	Urine Output	Uric Acid Excretion
4/16	82	96	52	6 a.m. to 8 a.m.	40	16
				8 a.m. to 10 a.m.	45	13.5
				10 a.m. to 12 m.	102	24.5
				12 m. to 2 p.m.	68	20.4
				2 p.m. to 4 p.m.	135	32
				4 p.m. to 6 p.m.	155	54.5
				6 p.m. to 8 p.m.	58	39
				8 p.m. to 6 a.m.	175	102
4/19	96	61	68	6 a.m. to 8 a.m.	30	44
				8 a.m. to 10 a.m.	65	38
				10 a.m. to 12 m.	115	31.5
				12 m. to 2 p.m.	150	13
				2 p.m. to 4 p.m.	160	21.5
				4 p.m. to 6 p.m.	135	32
				6 p.m. to 8 p.m.	75	23.5
				8 p.m. to 6 a.m.	215	205

CASE 3 (Tables 7, 8 and 9, Chart 3).—M. H., aged 10 years, observed over a period of twelve days, was kept on a diet consisting of several bran muffins and water for the first three days. For the next three days the diet consisted of protein, 75 gm.; fat, 60 gm.; carbohydrate, 65 gm. On the first day two hourly specimens of urine were collected and chemical determinations of the blood made. The remainder of the procedure was similar to the foregoing two cases.

TABLE 7 *(Case 3).—Summary of Findings*

	Diet				Body Weight, Kg.	Intake, C.c	Output, C.c.	Uric Acid Excretion, Mg.
Date	Protein	Fat	Carbohydrates	Calories				
6/10*	0	0	0	0	28.1	1,285	1,260	302
6/11		Same		Same	28.0	1,450	1,420	258
6/12		Same		Same	27.8	950	910	156
6/13*†	75	60	65	1,183	27.8	950	937	188
6/14		Same		Same	27.6	1,050	1,030	257.5
6/15†		Same		Same	27.7	1,300	1,290	283 5
6/16	100	68	54	1,264	27.7	1,150	1,140	358
6/17*†		Same		Same	27.8	1,050	1,016	403
6/18		Same		Same	27.9	1,220	1,200	300
6/19*	125	58	62	1,306	27.9	950	900	420
6/20		Same		Same	28.0	1,000	920	310
6/21		Same		Same	28.2	960	960	282

* Days on which chemical determinations on the blood were made.
† Days on which two-hour excretions of urine were collected.

TABLE 8 *(Case 3).—Chemical Determinations on the Blood*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
6/10	12	1.2	2.4	98
6/13	16	1.5	2.9	95
6/17	14	1.8	2.5	92
6/19	12	2.0	2.3	90

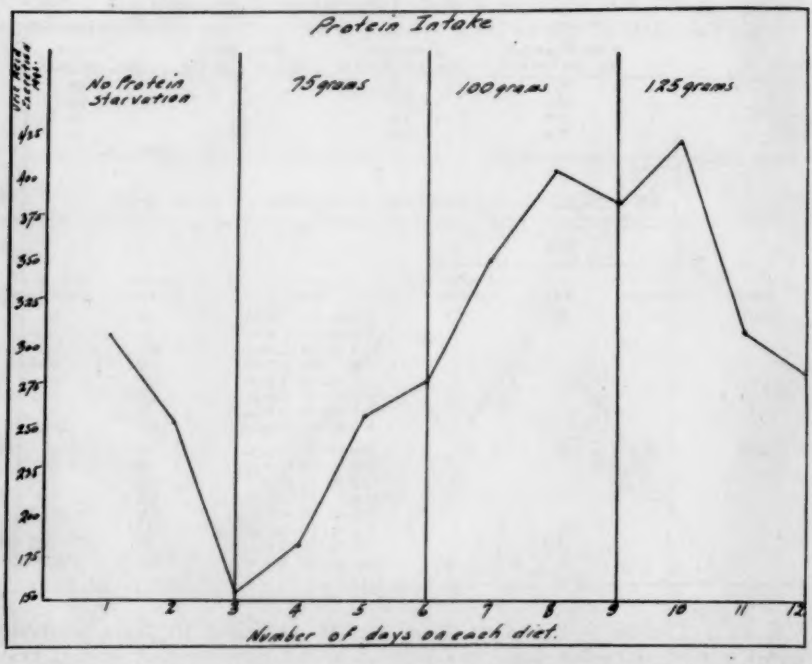

Chart 3.—Relationship between the protein intake and the daily uric acid excretion in Case 3.

TABLE 9 *(Case 3).—Two-Hour Excretions of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output	Uric Acid Excretion
6/13	75	60	65	6 a.m. to 8 a.m.	75	22.5
				8 a.m. to 10 a.m.	135	34
				10 a.m. to 12 m.	150	22.5
				12 m. to 2 p.m.	72	17
				2 p.m. to 4 p.m.	5	2
				4 p.m. to 6 p.m.	145	25
				6 p.m. to 8 p.m.	30	9
				8 p.m. to 6 a.m.	325	56
6/15	75	60	65	6 a.m. to 8 a.m.	60	14
				8 a.m. to 10 a.m.	100	25
				10 a.m. to 12 m.	190	30
				12 m. to 2 p.m.	230	28
				2 p.m. to 4 p.m.	140	34
				4 p.m. to 6 p.m.	155	39.5
				6 p.m. to 8 p.m.	90	28
				8 p.m. to 6 a.m.	325	85
6/17	100	68	54	6 a.m. to 8 a.m.	35	32
				8 a.m. to 10 a.m.	55	41
				10 a.m. to 12 m.	100	34
				12 m. to 2 p.m.	135	22
				2 p.m. to 4 p.m.	110	27
				4 p.m. to 6 p.m.	130	48
				6 p.m. to 8 p.m.	23	18
				8 p.m. to 6 a.m.	430	181

CASE 4 (Tables 10, 11 and 12, Chart 4).—S. K., aged 9 years, was observed over a period of twelve days. The procedure was similar to Case 3.

Chart 4.—Relationship between the protein intake and the daily uric acid excretion in Case 4.

TABLE 10 *(Case 4).—Summary of Findings*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrates	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.
6/10*	0	0	0	0	25.6	1,100	1,050	267
6/11		Same		Same	25.4	1,240	1,210	269
6/12		Same		Same	25.3	1,000	975	183
6/13*†	75	60	65	1,183	25.2	835	807	154.5
6/14		Same		Same	25.2	1,000	925	286
6/15†		Same		Same	25.2	1,100	1,067	265.5
6/16*	100	68	54	1,264	25.3	1,100	1,000	378
6/17†		Same		Same	25.3	900	882	341
6/18*		Same		Same	25.5	1,100	1,050	410
6/19	125	58	62	1,306	25.5	950	920	390
6/20		Same		Same	25.5	1,120	1,085	340
6/21		Same		Same	25.5	1,100	1,080	305

* Days on which chemical determinations on the blood were made.
† Days on which two-hour excretions of urine were collected.

TABLE 11 *(Case 4).—Chemical Determinations on the Blood*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
6/10	20	1.5	2.8	92
6/13	24	2.0	3.4	97
6/16	18	2.0	2.9	98
6/18	16	1.8	2.1	94

TABLE 12 *(Case 4).—Two-Hour Excretions of Uric Acid*

Date	Diet: Protein	Diet: Fat	Diet: Carbohydrate	Time	Urine Output	Uric Acid Excretion
6/13	75	60	65	6 a.m. to 8 a.m	30	5
				8 a.m. to 10 a.m	52	17
				10 a.m. to 12 m.	70	17
				12 m. to 2 p.m.	125	12
				2 p.m. to 4 p.m.	90	13.5
				4 p.m. to 6 p.m.	130	22
				6 p.m. to 8 p.m.	90	24
				8 p.m. to 6 a.m.	220	44
6/15	75	60	65	6 a.m. to 8 a.m.	15	6.5
				8 a.m. to 10 a.m.	120	34
				10 a.m. to 12 m.	170	30
				12 m. to 2 p.m.	260	41
				2 p.m. to 4 p.m.	140	28
				4 p.m. to 6 p.m.	120	48
				6 p.m. to 8 p.m.	80	24
				8 p.m. to 6 a.m.	162	54
6/17	100	68	54	6 a.m. to 8 a.m.	25	28
				8 a.m. to 10 a.m.	85	38
				10 a.m. to 12 m.	100	31
				12 m. to 2 p.m.	105	21
				2 p.m. to 4 p.m.	97	39
				4 p.m. to 6 p.m.	115	42
				6 p.m. to 8 p.m.	80	12
				8 p.m. to 6 a.m.	275	130

COMMENT

It will be noted that under the influence of increasing amounts of protein, a limit of uric acid excretion was gradually reached and that this maximum excretion varied for each case. An increase in the protein of the diet beyond this limit showed no corresponding increase in the uric acid elimination. In some cases (Cases 1, 2 and 3) such increase in protein resulted in a decreased elimination of uric acid. The increased uric acid output obtained on a purin-free high protein diet would suggest that such diets stimulate the elimination of endogenous uric acid. The failure of further increases in the protein portion of the diet to produce further increases in the uric acid excretion may be interpreted as a form of kidney "fatigue." This kidney "fatigue" further manifests itself by a fall in the uric acid excretion when the protein portion of the diet is still further increased. While the uric acid concentrations in the different specimens of blood examined showed only slight changes, we are inclined to believe that they are of sufficient importance to warrant discussion. In general, it was found that as the protein portion of the diet was increased, the uric acid of the blood decreased and that the lowest concentrations in the blood usually corresponded with the maximum excretion of uric acid in the urine. The fact that a high protein purin-free diet produces an increased daily elimination of uric acid, and at the same time reduces the concentration of the uric acid of the blood, below that obtained on a low protein diet, suggests a rather new rationale in the dietetic treatment of patients suffering from disturbances in the uric acid metabolism.

The present conception, with respect to the treatment of such disturbances, seems to point toward a restriction in the protein intake of the diet. Our results contradict this conception, and show that better results could be obtained by the addition of sufficient purin-free protein to the diet to produce a maximum excretion of uric acid. While this article was in preparation, the work of Folin and his co-workers [3] appeared reporting results similar to ours.

CONCLUSIONS

1. Gradually increasing the protein portion of the purin-free diets caused an increase in the uric acid excretion.

2. This increased excretion of uric acid reached a maximum which was different in each case, and any further addition of protein to the diet failed to cause a further increase in the elimination and in most cases caused a decrease.

3. The concentration of the uric acid in the blood decreased as the protein of the diet increased.

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3. Folin, O.; Berglund, H., and Derick, C.: J. Biol. Chem. **60**:361-471 (June) 1924.

ACIDIFICATION OF MILK WITH VINEGAR (ACETIC ACID) IN INFANT FEEDING *

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The rationale of adding an acid to cow's milk to improve its digestibility has been demonstrated by Clark [1] and Faber [2] and popularized recently by Marriott.[3] They show that the buffer value of cow's milk is considerably more than that of human milk. Therefore the former milk neutralizes a larger amount of the hydrochloric acid of the stomach. The resultant effect is an interference with the activity of the gastric enzymes through a reduction of the gastric acidity below the optimal hydrogen-ion concentration zone of p_H 3.5 to 5.0. By the addition of an acid to cow's milk its excess buffer salts may be counteracted, and its digestibility made to simulate more nearly that of human milk. This method does not entail any appreciable reduction of the food elements, as pertains to the ordinary method of simple dilution.

The question as to what degree of acidification of the milk is most efficacious, as well as which acid is best for this purpose, is still an open one. Faber [2] used hydrochloric acid because it is the physiologic one. His best results were obtained from a formula, the buffer value of which was reduced to about that of human milk. The p_H of the mixture was 6.0 in contrast to 6.6 for cow's sweet milk. The product was not considered suitable for infants under 6 weeks of age.

Marriott [3] used lactic acid because it is the one of bacterially soured milk. He employed a formula with a value of p_H 4.0. The mixture was recommended for infants of all ages.

The addition of citric acid in the form of lemon juice was advocated by Hess [4] because of the contained antiscorbutic vitamin. Citric acid in small quantities is also a normal constituent of milk. A two-thirds dilution of acidulated milk was used. The resultant acidity was p_H 5.3. The mixture was not thought to be advisable for infants aged less than 2 months.

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* Received for publication, Dec. 9, 1924.

1. Clark, W. M.: The Reaction of Cow's Milk Modified for Infant Feeding, J. M. Res. **31**:431, 1914.

2. Faber, H. K.: Hydrochloric Acid Milk in Infant Feeding, Am. J. Dis. Child. **26**:401 (Nov.) 1923.

3. Marriott, W. M., and Davidson, L. T.: Acidified Whole Milk as a Routine Infant Food, J. A. M. A. **81**:2007 (Dec. 15) 1923; The Acidity of the Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

4. Hess, A. F., and Matzner, M. J.: The Value of Milk Acidified with Lemon Juice, J. A. M. A. **82**:1604 (May 17) 1924.

Within certain age limits, all of the foregoing acids have given satisfactory results. Owing to wide variations in the degree of acidity employed for the respective acids, as well as the combined use of simple dilution, a true evaluation of the relative merits of each acid cannot be made from a comparison of the clinical results. Neither can conclusions be made as to what is the optimal degree of fortified acidity. Rather, in some instances, the amount of acid used may represent only the dosage limit for that particular acid. However, it may be pointed out that lactic acid was tolerated at an earlier age, in a higher degree of acid concentration, and without dilution of the milk. From these observations it may be inferred that the status of an acid as a physiologic one or as a normal constituent of milk need not necessarily be considered a criterion for suitability as an acidifying agent. Other things being equal, it is obvious that the acid of choice should be one which itself, or whose combination products with milk, is easily utilized by the organism in whatever quantity may produce the ideal fortified acid value to the mixture. The resulting curd should be fine and flocculent. The mixture should be acceptable to the infant; also the factors of cost, availability and safety as an article for use in the kitchen may well be considered.

In searching for an acid that would conform with the preceding conditions, I used dilute acetic acid in the form of ordinary household vinegar. Bottled apple cider vinegar of a brand [5] having a wide distribution in the grocery trade was used principally in this work. Vinegar is made from the expressed juice of fruits under the control of the Federal Food Laws and licensure of the Volstead Act.[6] The chemical process consists primarily of a conversion of fruit sugar to alcohol by yeast, and secondly of oxidization of the alcohol to acetic acid by bacterial fermentation. After aging and filtering, the product, vinegar, represents a weak solution of acetic acid (from 5 to 6 per cent. acid) with variable traces of other ingredients, which seem harmless to the infant.

Various ratios of vinegar and milk were tried. The one that gave most constantly satisfactory results was 1 ounce (30 c.c.) of vinegar to 15 ounces (450 c.c.) of cow's milk. Expressed in terms of their equivalent values for use in the home, this equaled 1 common teaspoonful of vinegar to each 3 ounces of milk in the formula. For the convenience of the hospital dietitian the schedule in the table was used. The acetic

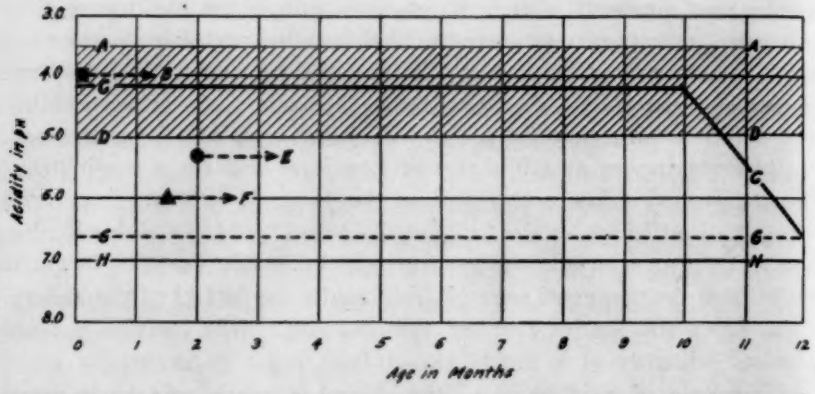
5. Heinz's "pure apple cider vinegar" was used. The chemical analysis by the manufacturer is as follows: Acetic acid, from 5.0 to 6.0 per cent.; alcohol, from 0.0 to 0.4 per cent.; lactic acid, from 0.08 to 0.12 per cent.; reducing sugars, from 0.4 to 0.6 per cent.; glycerin, from 0.2 to 0.4 per cent.; ethyl acetate, from 0.3 to 0.9 per cent., and phosphates, from 0.028 to 0.032 gm.

6. U. S. Treasury Department, Bureau of Internal Revenue, Washington, D. C.: Regulations 60 Relative to Intoxicating Liquor, pp. 63, 66, 67; and U. S. Department of Agriculture, Washington, D. C., Farmer's Bulletin 1424 and Food Inspection Decision 140.

Vinegar Milk Schedule for Dietitians

Vinegar Milk, Ounces		Milk, Ounces		Vinegar, Ounces	Vinegar Milk, Ounces		Milk, Ounces		Vinegar, Ounces
16	=	15	+	1	2	=	1 7/8	+	0 1/8
32	=	30	+	2	4	=	3 6/8	+	0 2/8
48	=	45	+	3	6	=	5 5/8	+	0 3/8
64	=	60	+	4	8	=	7 4/8	+	0 4/8
80	=	75	+	5	10	=	9 3/8	+	0 5/8
96	=	90	+	6	12	=	11 2/8	+	0 6/8
112	=	105	+	7	14	=	13 1/8	+	0 7/8
128	=	120	+	8					

acid addition to the mixture was one-third per cent. The hydrogen-ion concentration of the mixture was about p_H 4.2. This ratio was used until about the tenth month of age, after which in healthy infants the vinegar



Relative acidity in p_H of vinegar milk. A to D, zone of effective gastric digestion; B, Marriott's lactic acid milk; C, vinegar (acetic acid) milk; E, Hess' lemon juice (citric acid) milk; F, Faber's hydrochloric acid milk; G, cow's sweet milk; H, neutrality.

milk was gradually replaced by sweet milk, and the former was entirely omitted by the end of the first year. The p_H of vinegar milk in relation to the zone of effective gastric digestion and in comparison with other types of acidified milk is shown in the chart.

The curd of vinegar milk of the foregoing description is fine, smooth and flocculent. After the preliminary shaking of the mixture there is no further separation into whey and curds during the nursing period. The taste is agreeable with a faint, apple cider flavor. At the present retail price of vinegar (35 cents per quart),[5] vinegar milk may be produced in the home at about 1 cent per pint. Barreled vinegar of equivalent strength from the hospital diet kitchen[7] reduced the cost to one-sixth cent per pint for the institution babies.

7. Maternity and Children's Hospital.

The chemistry and metabolism of acetic acid and its salts are similar to those of the other organic acids. The basic buffer substances of the milk unite with the acetic acid of the vinegar to form the various acetates of sodium, potassium, magnesium, and so forth. These salts are very soluble. They are rapidly absorbed from the intestine and are rapidly and completely oxidized in the tissues to the bicarbonates, carbon dioxid and water.[8] The bicarbonates are eliminated by the kidneys. Large doses may exert an alkaline diuretic effect. In testing the action of acetic acid on rats, Sollmann [9] fed massive doses of 0.25 per cent. of the acid, equivalent in man to 8 ounces (236 c.c.) of vinegar (5 per cent. acid), daily for several months. There were no adverse results, not even diuresis. Only double this quantity produced material and progressive interference with appetite and growth.

Admittedly, the final judgment of the value of any preparation must be based on the reaction of the infant to the food. However, some advantages of acetic acid modification of milk over other organic acids may be inferred from the following facts. The acetates are more readily absorbed from the intestine than the lactates, citrates and others of the group [8] and hence have less laxative properties.[9] The acetates do not inactivate calcium, as do the citrates, tartrates and oxalates.[9] The acetates exert no poisonous ion action in the blood stream, as pertains to the oxalates and tartrates.[9] In fact the acetates seem almost devoid of any specific action,[8] and there appears to be no counterindication to their use.

In round numbers, the amount of vinegar milk prescribed for each infant was usually from 2¾ to 2¼ ounces per pound of body weight for those weighing under 14 pounds. The daily quantity of vinegar milk was from 16 to 32 ounces (480 to 960 c.c.). The latter amount was usually given to babies of average development about the fifth month of life. This milk-weight ratio usually satisfied the hunger and maintained a satisfactory rate of growth. The vinegar milk was given undiluted, except to infants younger than 2 months who received 4 ounces (120 c.c.) of water or gruel in the total daily feeding.

Corn syrup previously diluted with an equal volume of water was added in the usual amount of 1 ounce (2 tablespoonfuls, 30 c.c.) of the diluted syrup, about one-half ounce (17 gm.) of carbohydrate by weight, to the pint of vinegar milk. The total daily addition of diluted syrup seldom exceeded 1½ ounces (45 c.c.), and this was usually reduced after cereals were begun.

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8. Cushny, A. R.: A Textbook of Pharmacology and Therapeutics, Ed. 5, pp. 557, 560, 1913.
9. Sollmann, T.: Manual of Pharmacology, Ed. 2, pp. 851, 854, 1922.

The preparation of vinegar milk was similar to that of other acidified products. The milk was previously sterilized, the syrup was added and the milk was thoroughly cooled before the vinegar was stirred into the mixture. A cool temperature was continued until the time for the moderate degree of warming before feeding. Four-hour feeding intervals were used.

Spoon feedings of cereal gruel and vegetable mash were usually given before feedings to well babies after the third and fifth months, respectively. The cereal was offered twice daily, in amounts increasing to 3 or more ounces (90 c.c.) of 6 per cent. gruel per feeding in accordance with the appetite. The vegetable was given once daily in about one-half the quantity of a cereal feeding. Extra water was offered between meals. Orange juice and cod liver oil were given routinely as soon as the digestive condition permitted.

CLINICAL RESULTS

Some forty infants, chiefly of hospital and dispensary type, have been under observation on vinegar milk mixtures for periods of from one to six months throughout the last year. In no instance was it found necessary to change the type of feeding. The ages at the time of beginning the mixture have ranged from 4 days to 22 months. The diagnoses include boarding babies, regulation of diet, infantile atrophy, pylorospasm, syphilis, rickets and parenteral infections. The general appearance, contentment, nutrition, tissue turgor, musculature and rate of growth of the infants compare favorably and in general parallel those on lactic and citric acid mixtures. The digestion was good. Neither vomiting nor flatulency was unduly encountered. Substitution of vinegar either for or by the other acids was sometimes made without noticeable change of clinical signs. Refusal of the mixture was not observed in any of the hospital cases. The stools usually averaged from two to three daily and were of soft yellow consistency without free fat.

In some instances where the amount of vinegar was less or the quantity of syrup was more than that recommended, frequency of stools and intertrigo of the buttocks occurred. A return to the normal proportions usually promptly effected a return to the normal digestion. Occasionally intercurrent parenteral infections were accompanied by indigestion with free fat in the stools. Replacement of the whole vinegar milk by skimmed vinegar milk and a reduction or temporary omission of the syrup was the dietary alteration of choice. In well babies changes in formulas were very infrequent. Usually one mixture would suffice for a period of four to six weeks before another raise of from 2 to 4 ounces (from 60 to 120 c.c.) of vinegar milk was necessary.

SUMMARY AND CONCLUSIONS

Acetic acid has been added to cow's milk to counteract the effect of the buffer substances of the milk on the gastric acidity. The usage of this acid in the form of ordinary household vinegar lessened the cost of acidulation, utilized a common and harmless article of the kitchen for this purpose, and made the grocery store the source of supply.

A pint of vinegar milk was made from 1 ounce (30 c.c.) of vinegar (from 5 to 6 per cent. acetic acid) to 15 ounces (450 c.c.) of cow's milk. The vinegar milk was given undiluted, except to infants younger than 2 months who received 4 ounces (120 c.c.) of water or gruel in the total daily feeding. Corn syrup diluted with an equal volume of water was added in the amount of 1 ounce (30 c.c.) of the diluted syrup to the pint of vinegar milk. The daily amount of the diluted syrup seldom exceeded 1½ ounces (45 c.c.), and this was reduced after cereal feedings were begun. The foregoing mixture was well tolerated as a routine food. Disturbance of the digestion was a rare occurrence, and was correctable by a temporary reduction of the sugar and fat elements of the food.

The clinical results of vinegar milk feeding compare favorably with those of other types of acidified milk. The factors of economy, common usage, wide commercial distribution and safety recommend vinegar for the acidifying agent when acidified milk is indicated.

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GONORRHEAL PROCTITIS AS A CAUSE OF BLOOD AND MUCUS IN THE STOOLS OF INFANTS*

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There are many causes which, in infants, give rise to the presence of blood and mucus in the stool, the most common one being infection of the alimentary tract. The following series of cases is concerned with children in whom the blood and mucus were due to infection of the rectum by the gonococcus.

REVIEW OF THE LITERATURE

Gonorrheal proctitis has long been recognized as an entity, particularly abroad, although there are also reports of cases from this country. Rollet [1] in 1871, Potherat [2] in 1892, and Troncay [3] were among the first to describe the condition. Opinions differ as to its incidence in children. Flugel,[4] in the course of a routine examination of fifty-six children with vulvovaginitis, found proctitis in eleven instances. Holt,[5] among 233 children, encountered no case with gonorrheal infection of the genital tract. Pollack,[6] among 189 children with vaginitis, found seven with rectal complications. Spaulding [7] reported six cases of rectal infection in seventy-four girls with vaginitis. Gant [8] states: "Venereal disease in the anorectal region is quite common—gonorrhea is most active in the anal canal and occasionally involves the upper rectum." Kaumheimer [9]

* Received for publication, Dec. 4, 1924.

* From the Home for Hebrew Infants.

1. Rollet: Maladies veneriennes de l'anus, Dictionnaire Dechambre **5**:491, 1871.

2. Potherat: Rectite blennoragique—traite de chirurgie de duplay et reclus, 1892.

3. Troncay: Etude sur la blennoragie ano-rectale, Thèse Nancy, 1897.

4. Flugel: Cited by Kaumheimer, footnote 9.

5. Holt, L. E.: Gonococcus Infections in Children, New York M. J. **81**: 521-589 (March 18) 1905.

6. Pollack: The acquired Venereal Infection in Children, Bull. Johns Hopkins Hosp. **20**:142 (May) 1909.

7. Spaulding, E. R.: Vulvovaginitis in Children, Am. J. Dis. Child. **5**:248 (March) 1913.

8. Gant: Diseases of the Rectum, vol. 2, p. 179.

9. Kaumheimer: Ueber Rectal Gonorrhae im Kindesalter, München med. Wchnschr. **17**:963, 1910.

presented in detail the clinical picture of a case of gonorrheal proctitis which had been followed carefully from day to day, and which presented the typical symptoms of many intestinal infections, namely, the passage of loose stools with mucus. Lauter [10] stated that ten among fifteen newly admitted children with gonorrhea and seven among thirteen old cases, presented macroscopic changes in the rectal mucous membrane, chiefly in the form of membranes. In all these cases leukocytes and gonococci were found in almost every smear and at every examination.

ETIOLOGY

None of these authors mentions the presence of blood in the stools as evidence of active gonorrheal disease of the rectum. In our series this was the most striking sign. Probably this can be accounted for by the fact that most of the infants in the group were under 2 years of age, whereas in the other reports they were older. The intestine of the young infant is more susceptible to infection, and the infection is more apt to produce serious changes in the mucosa. This group of forty-one cases of active gonorrheal proctitis in children is the largest series that has been reported. Only those cases have been included in which the signs of rectal infection have been confirmed by microscopic examination.

Some time ago several children in one of the wards began to pass bloody stools, which persisted in spite of dietary treatment for colitis. Examinations of the stools for dysentery bacilli were repeatedly negative. The milk used in the diets was pasteurized, and its bacterial count was found to be very low. The cause and source of the infection were obscure. Following irrigations with a silver nitrate solution, 1 : 3,000, the condition cleared up after a few weeks.

Soon after, several cases of this condition developed in another ward, in which female infants who showed gonococci by vaginal smear were kept. A smear was then taken from the rectum of every infant who was passing blood, and numerous pus cells containing gram-negative intracellular diplococci were found. Subsequently, in every child who developed blood in the stools, similar smears were taken and all showed the same picture. A male infant who had been having such stools developed acute urethritis about seventeen days after the onset of the proctitis. The situation was now clear and we initiated treatment early in the subsequent cases.

There were forty-one cases in all. Ten of these were males, among whom three developed acute urethritis during the course of the proctitis. In the female infants acute vulvovaginitis (cervicitis) was present usually at the time of the infection, although in one instance the rectal infection

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10. Lauter, L.: Rectal Findings in Gonorrhea in Children, Deutsch. med. Wchnschr. **48**:1285 (Sept. 22) 1922.

preceded its onset. The ages of the infants varied from 5 months to 3 years.

METHOD OF INFECTION

The method of infection has been ascribed generally to contact with various contaminated articles, such as bathing water, towels, washcloths, thermometers and rectal irrigation tips. We found an additional source of infection to be the sheet covering the "changing table." When the diapers were removed and while fresh ones were being procured, the infant sat up or lay on the table uncovered, so that when the next child was placed on the table it came in contact with any infective secretions present. This source of infection was eliminated by placing a diaper on top of the sheet and having it renewed for each child.

SIGNS OF INFECTION

The first sign of infection was the presence of mucus in the stools, which shortly thereafter became loose and green. The number of bowel movements was only slightly increased. Later blood appeared in varying amounts, mixed with feces and mucus. Pus was present also, although distinguished macroscopically with difficulty. In many of the patients there was no rise of temperature, but fever was present in several at the onset. This was usually due to some general infection such as grip, tonsillitis or measles. It is probable that in these infants the organisms had long been present in the rectum, and that the acute illness precipitated the attack of proctitis. After the acute illness had subsided, there was usually little rise of temperature throughout the course of the rectal infection, notwithstanding the fact that the blood and mucus continued to be present in the stools. It is well known that vaginitis is activated by acute febrile diseases, and proctitis may be affected likewise. In this connection it may be noted that Hess [11] reported the use of "provocative vaccination" by means of a nonspecific vaccine to produce an active discharge in suspected cases of vaginitis. In this way latent cases were activated, the diagnosis could be established and further infection prevented. Incidentally, the same author pointed out that "vulvovaginitis" in reality is cervicitis, basing this conclusion on the microscopic examination at necropsy of the genital tracts of four infants with vaginitis.

TREATMENT

On direct examination of the rectum, marked congestion of the mucous membrane was found, with a decided tendency to prolapse. In one case this condition was so severe that the buttocks had to be kept

11. Hess, A. F.: Provocative and Prophylactic Vaccination in the Vaginitis of Infants, Am. J. Dis. Child. **12**:466 (Nov.) 1916.

strapped together with adhesive strips. There was also considerable tenesmus. Proctoscopic examination showed the congestion of the mucous membrane to extend high into the rectum, and revealed the presence of marked ulceration even 3 and 4 inches (7 and 10 cm.) from the anus.

Under irrigations with solutions of silver nitrate, 1: 3,000, the symptoms cleared up more or less quickly, the stools resuming their normal character in two or four weeks. The mucus, however, persisted for much longer periods. Two patients which were supposedly cured came to necropsy, having died of intercurrent pneumonia. Examination of the rectum showed extensive ulceration, extending in one case 6 inches (15 cm.) and in the other 4 inches (10 cm.) from the anal margin. The ulcers varied in degree, the largest being fully 1 cm. in diameter and penetrating to the muscular coat. Thus the condition was much more serious than had been supposed, since there had been an apparent clinical cure. In this connection it is significant to note that Weissman [12] found gonorrheal proctitis to be occasionally very resistant to treatment, to such an extent as to render colostomy necessary. Symonds [13] has reported a case of stricture of the rectum due to infection by the gonococcus. In subsequent cases we used irrigations of acriflavin, 1: 1,000. This caused rapid disappearance of the organisms but not of the blood. We used this treatment alternately with the silver nitrate irrigations, with results which seemed better in the few patients in which we had the opportunity to test the procedure. Although treatment of this kind seemed successful, proctoscopic examination of these patients two and three months later revealed ulcers still present in many instances. For this reason we wish to emphasize the importance of early diagnosis, in order that proper treatment may be instituted before marked destruction of tissue has ensued.

ISOLATION OF BACTERIA

In a few cases, attempts were made to isolate the gonococcus from cultures of the rectum. When simple swabbing was carried out to obtain the material for culture, other organisms overgrew the gonococci. Later, however, in five instances the material was obtained directly from the ulcers through the proctoscope, and from two of these the gonococcus was isolated. For this work we are indebted to Miss May Wilson, bacteriologist to the Willard Parker Hospital.

Routine rectal smears were taken on 125 children, of whom eighty-six, or about two-thirds, were girls and thirty-nine were boys. Only

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12. Weissman, L.: Gonococcus Infection of Anus and Rectum, J. d'urol. méd. et chir. **15**:31 (Jan.) 1923.

13. Symonds, C.: Gonorrheal Stricture of the Rectum, Proc. Roy. Soc. Med. **16**:12-20 (Jan.) 1923.

eight were positive for gonococci and five of these were smears from female infants. This entire group of girls showed gonococci on vaginal smears but no child had an active discharge. The wearing of diapers seems to be an important factor in the incidence of the infection. Of the 125 children, sixty-six were under 2 years of age, and seven of the eight positive rectal smears were from children belonging to this group. Of the forty-one proctitis cases, thirty-seven belonged to the same group who wore diapers. It can readily be imagined that where there is an active vaginitis the diaper keeps the secretions in contact with the rectum, so that infection can scarcely be avoided.

The fact that gonococci continually gain access to the rectum and cause reinfection is probably an important cause of failure of treatment of so many cases of vaginitis. In this connection Valentin's [14] experience in the treatment of 161 cases of infantile gonorrhea may be referred to; almost all the children had recurrences and in sixty-one the gonococci were found to persist in the rectum.

In the smears of the active cases pus cells and cocci are readily found, but in the latent cases a thorough search must be made, as the smear is often composed of fecal matter which renders difficult the finding of the gonococci which are less numerous than in the acute cases. In taking smears from girls with profuse vaginal discharges, the greatest care must be observed not to allow the secretions to contaminate the rectum; smears were taken high in the rectum so as to be certain of this source.

REPORT OF CASES

CASE 1.—A boy, aged 25 months, was perefectly well until January 24, when he developed a sore throat. Examination of the throat showed that the patient had a severe attack of Vincent's angina. Intramuscular injections of sulpharsphenamin were given. One week later he began to pass stools containing blood and mucus. He was given castor oil, and a diet of protein milk and broth, as well as 1 dram of kaolin every three hours. The colon was irrigated daily with physiologic sodium chlorid solution. Examination of the stools for dysentery bacilli was negative. There was no improvement after fourteen days' treatment and colonic irrigations of silver nitrate, 1 : 3000, were instituted. Within a week the stools had resumed their normal consistency. Subsequently, seventeen days after the appearance of blood in the stool, the boy had developed an acute urethritis which proved to be gonococcal in origin. Smears from the rectum also showed the presence of gonococci.

This illustrates how the patient was treated as a simple case of enterocolitis. The diagnosis became apparent only on the appearance of the urethritis. The Vincent's angina seemed to precipitate the proctitis. As the symptom appeared within a week of the child's removal to the infirmary, the infection could not have been contracted there, so that the organisms must previously have been present in the rectum.

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14. Valentin, J. E.: Recurrence in Infantile Gonorrhea, Deutsch. med. Wchnschr. **47**:628 (June 2) 1921.

CASE 2.—E. S., a girl, aged 15 months, seemed perfectly well except for the fact that she was passing blood in the stools. She had at the time active vulvovaginitis. Smears from the rectum showed gonococci to be present. The colon was irrigated once daily with silver nitrate 1:3000. No change was made in the diet. After fourteen days the condition cleared up. Throughout this time the temperature never rose above 99.6 F., and the number of stools was never more than two daily.

This was an uncomplicated case of proctitis. It showed the lack of fever and other systemic symptoms. The first indication of infection was the presence of blood in the stools. A prompt diagnosis enabled us to effect a cure in two weeks.

Forty-One Cases of Gonorrheal Proctitis Showing Blood and Mucus in the Stools

Case	Sex*	Age, Months	Date	Ward	Associated Gonococcus Infection	Duration, Days
1	♀	9	Jan. 28	B	Vaginitis	14
2	♂	28	Jan. 31	A	Urethritis†	21
3	♀	6	March 18	A	Vaginitis	23
4	♀	10	March 18	A	Vaginitis	40
5	♀	13	March 18	A	Vaginitis	24
6	♀	15	March 19	A	Vaginitis	15
7	♀	24	March 19	A	Vaginitis	30
8	♂	13	March 19	A	None	6
9	♂	7	March 20	A	None	13
10	♀	17	March 22	A	Vaginitis	14
11	♂	24	March 22	A	Urethritis†	18
12	♂	7	March 26	A	None	20
13	♀	24	March 26	C	Vaginitis	30
14	♀	15	March 26	A	Vaginitis	30
15	♀	22	April 1	C	Vaginitis	18
16	♀	24	April 1	C	Vaginitis	19
17	♀	21	April 1	C	Vaginitis	21
18	♀	19	April 10	C	Vaginitis	30
19	♀	26	April 14	C	Vaginitis	21
20	♂	19	April 24	A	None	35
21	♀	15	April 28	A	Vaginitis	17
22	♂	16	April 30	C	Urethritis†	10
23	♂	23	May 2	D	None	20
24	♂	19	May 7	C	None	17
25	♀	18	May 7	D	None	31
26	♂	16	May 11	D	None	21
27	♀	21	May 16	D	Vaginitis†	18
28	♀	17	May 17	D	Vaginitis	20
29	♂	18	May 17	D	None	30
30	♀	21	May 19	D	Vaginitis	21
31	♀	15	May 28	C	Vaginitis	35
32	♀	16	May 30	C	Vaginitis	26
33	♀	26	June 7	C	Vaginitis	14
34	♀	27	June 13	E	Vaginitis	20
35	♀	26	June 13	D	Vaginitis	19
36	♀	19	June 16	A	Vaginitis	4
37	♀	15	June 24	C	Vaginitis	14
38	♂	17	June 27	D	None	29
39	♀	15	June 29	A	Vaginitis	16
40	♀	15	Aug. 28	A	Vaginitis	32
41	♀	18	Oct. 24	A	Vaginitis	..

* In this column, ♀ indicates female; ♂, male.
† In these, the proctitis preceded the infection of the genital tract.

CASE 3.—H. Z., a boy, aged 3½ years. Our attention was drawn to this child because of the presence of blood in the stools. Smears from the rectum showed the gonococci to be present. He was immediately given daily irrigations of silver nitrate, 1:3000. No change was made in the diet. The temperature throughout did not rise above 99.6 F., and there were never more than two stools daily. Culture from the rectum was positive for gonococcus. After three weeks' treatment, he still continued to have small amounts of blood in the stools, which otherwise were normal. Proctoscopic examination showed the presence of several ulcers extending as far as 3 inches (7 cm.) from the anal margin. This case again illustrates the lack of general reaction although the local lesion was quite extensive. Here, although treatment was instituted fairly early, it was

not successful. This boy was in a ward with other boys and there was no contact with cases of vaginitis. He may have had the infection before admission, for a sister, aged 4 months, had a positive vaginal smear on admission.

COMMENT

The first question which arises is why so many cases of this disease have developed at this period, whereas formerly only an occasional case of this kind has been observed. This is due to the fact that until recently girls with vaginal gonococci were not admitted to the institution. The result was that there were few girls with vaginitis in the Home, although in spite of every precaution an occasional one would slip in. Recently, however, this regulation was changed, so that infected girls are admitted. Now the chances for infection are innumerably greater, although all precautions are observed to segregate these children. In view of the fact that it is frequently assumed that vaginitis is essentially an institutional disease, our recent experience should be of interest; forty-seven out of eighty-nine girls over 1 year of age showed gonococci on admission in routine vaginal smears. Under 1 year only thirteen out of eighty-six had positive smears. Bland,[15] among others, states that gonorrheal infection in children is common in private practice. We have observed one definite case of proctitis in a child on admission, characterized by congestion of the rectal mucosa, a slight prolapse and gram-negative intracellular diplococci.

In institutions it is the latent case that causes most of the trouble, the case in which the organisms remain undetected either in the vagina or in the rectum. These children are placed in the "clean" wards, and with the occurrence of a slight general infection, such as grip, the vaginitis flares up and infects others.

Clinically proctitis somewhat resembles ulcerative colitis, and it is quite possible that some of the cases of "idiopathic" ulcerative colitis are gonococcal in origin. Helmholz,[16] in reporting cases of chronic ulcerative colitis in children, mentions one which had complicating arthritis and conjunctivitis. Crohn and Rosenberg[17] report favorable results with acriflavin in the treatment of chronic ulcerative colitis. It would have been of interest to have had bacteriologic data on these cases, as this drug is known to exert a strong germicidal action on the gonococcus.

Prolapse of the rectum on straining occurred very often in these infants. It is not improbable that some cases of prolapse of the rectum

15. Bland, P. B.: Gonorrheal Infection in Childhood, New York M. J. **111**: 489 (March 20) 1920.

16. Helmholz, H. F.: Chronic Ulcerative Colitis in Childhood, Am. J. Dis. Child. **26**:418 (Nov.) 1923.

17. Crohn, B. B., and Rosenberg, Herman: The Medical Treatment of Chronic Ulcerative Colitis (Nonspecific), J. A. M. A. **83**:326 (April 2) 1924.

in children, especially if accompanied by blood in the stools, may be due to gonococcus infection.

SUMMARY

Gonorrheal proctitis in infants may give rise to the presence of blood and mucus in the stools. In a series of forty-one cases in which bloody stools was the striking sign, smears from the rectum of every child showed the presence of numerous pus cells, containing gram-negative intracellular diplococci. Repeated cultures for dysentery bacilli were negative. The majority of the infants were female, and almost every one had an active vaginitis associated with the rectal infection. In three of the male babies, acute urethritis developed during the course of the proctitis. In two cases the gonococcus was isolated in culture from the ulcers in the rectum.

The infection produces serious pathologic ulceration and is very resistant to treatment. It is therefore important that the diagnosis be made early, so that treatment may be instituted before marked destruction of tissue has occurred.

It is suggested that some cases of chronic "idiopathic" ulcerative colitis are due to a gonococcus infection.

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ANTITOXIN INTRAPERITONEALLY *

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In 1917, Fonde [1] reported a case of malignant diphtheria, treated by massive doses of antitoxin given intraperitoneally. In November, 1921, Goehle and Dauer [2] from this hospital reported five additional cases, treated intraperitoneally with diphtheria antitoxin mixed with saline solution, a procedure initiated, because one of the authors had the impression that antitoxin given intravenously in patients severely ill, was followed often by serious results. Recently Platou [3] published his observations on twelve cases of diphtheria treated in the same way, but with a specially made globulin antitoxin mixed with saline solution. In the last year, fifty cases of diphtheria have been treated with commercial antitoxin, injected intraperitoneally without the admixture of saline solution. We are reporting these cases and are comparing them with 100 other cases of diphtheria; fifty of the patients were treated with intramuscular and fifty with intravenous injection of diphtheria antitoxin.

Chart 1 shows the pulse record after injection. On admission, the highest pulse rate of the patient was, intramuscularly, 170; intravenously, 180, and intraperitoneally, 184. The lowest pulse rate was, intramuscularly, 80; intravenously, 84, and intraperitoneally, 80.

Chart 2 graphically illustrates the abrupt rise in temperature after the intravenous injection of diphtheria antitoxin, the average increase being 1.2 degrees, while with the intramuscular injection of diphtheria antitoxin there was practically no rise from the initial temperature, either immediately or within an hour after the injection. In the cases treated with antitoxin intraperitoneally, there was an average increase of 0.2, occurring within an hour after the injection. In two instances where intravenous antitoxin was given the temperature increased 4.5 degrees.

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* Received for publication, Nov. 10, 1924.

* From the Division of Contagious Diseases, Cleveland City Hospital, and the Department of Pediatrics, Western Reserve University.

1. Fonde, G. H.: Malignant Diphtheria, Internat. Clin. **3**:198, 1917.

2. Goehle and Dauer: Antitoxin Intraperitoneally. Central States Pediatric Association, November, 1921. (Transactions not published.)

3. Platou, E. S.: Antitoxin in Diphtheria, Arch. Pediat. **40**:575 (Sept.) 1923.

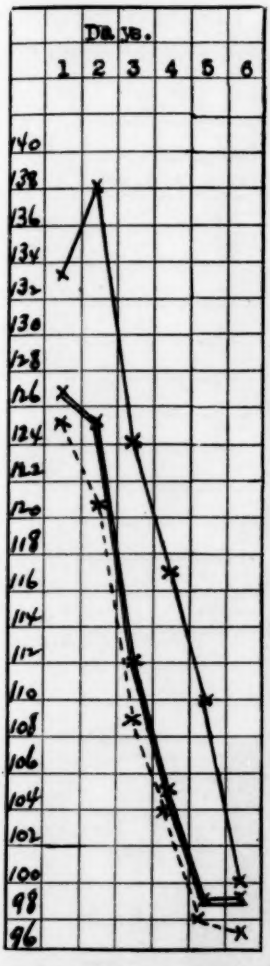

Chart 1.—Pulse record after injection; the broken line shows the intramuscular injection, the double line shows the intravenous injection, and the straight line shows the intraperitoneal injection.

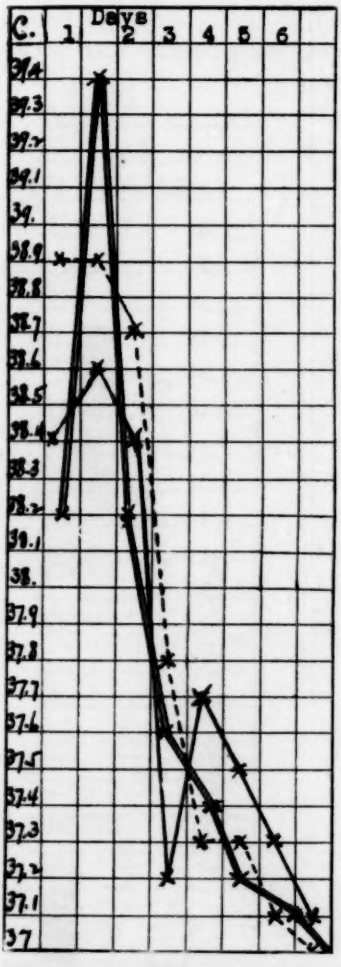

Chart 2.—Temperature record one hour after antitoxin was given, where there was no chill or at the height of the chill, when that was present. The highest temperature after intramuscular antitoxin injections, indicated by the broken line, was 40.8 C.; after intravenous injection, indicated by the double line, 42.4 C.; after intraperitoneal injection 41.6 C.

Chart 3 indicates the length of time pain lasted after intramuscular injections.

In no case was there pain at the site of injection after seventy hours, as can be seen by referring to Chart 4. In children the pain disappears more rapidly than with adults, averaging approximately thirty-six hours.

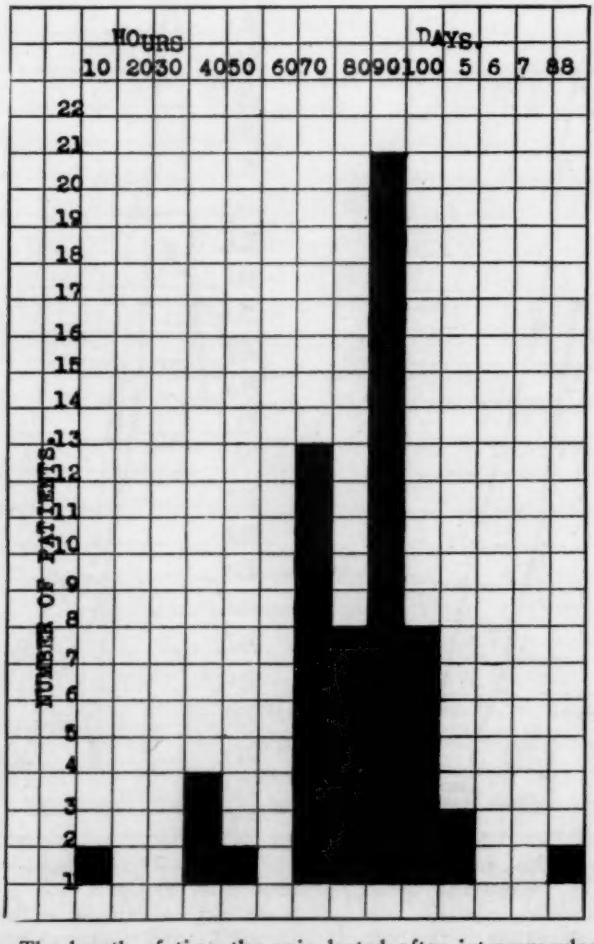

Chart 3.—The length of time the pain lasted after intramuscular injection.

Twelve additional patients were each injected intraperitoneally and intramuscularly at the same time on their admission, in order to ascertain the relative intensity of pain at the site of either injection. The results are found in Chart 5.

As we have stated, the chill associated with the injection of a foreign protein sometimes is so great as, in our opinion, to hurry on to a fatal

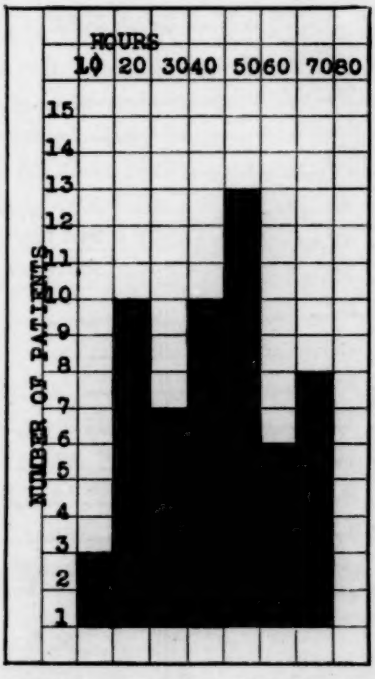

Chart 4.—The length of time the pain lasted after intraperitoneal injection.

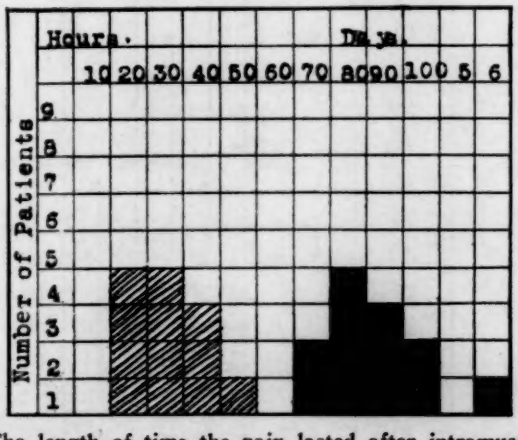

Chart 5.—The length of time the pain lasted after intramuscular injection of 20,000 units of antitoxin, indicated by the light squares; the length of time the pain lasted after intraperitoneal injection of the same quantity of antitoxin is indicated by the heavy squares.

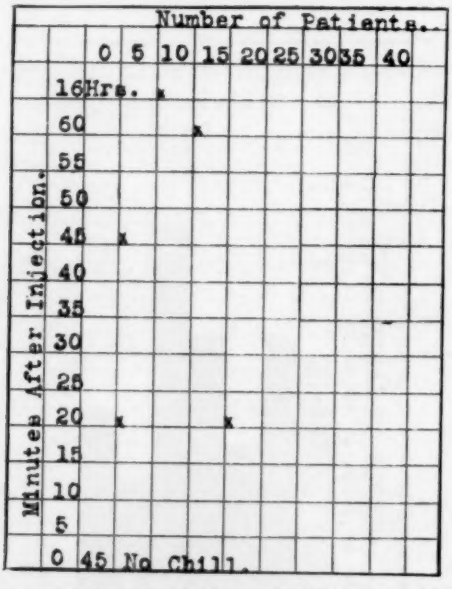

Chart 6.—Number and length of time of chills after intramuscular injection. The average length of chill lasted for 10.5 minutes. Ten per cent. of the patients had chills.

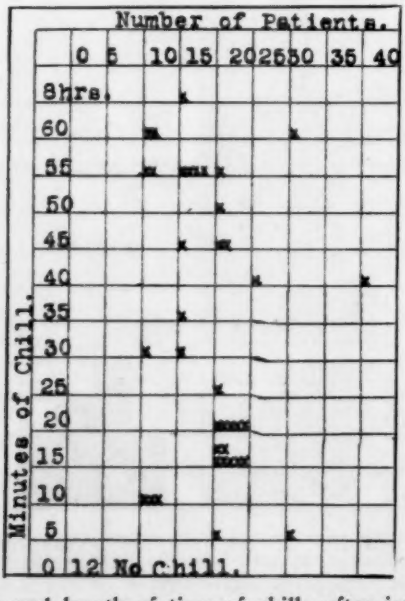

Chart 7.—Number and length of time of chills after intravenous injection. The average length of chill lasted for 17.7 minutes. Seventy-six per cent. of the patients had chills.

issue patients extremely ill with diphtheria, especially those associated with a toxic myocarditis. In Charts 6, 7 and 8, we tabulated the number and length of times chills occurred after intramuscular, intravenous and intraperitoneal injections of antitoxin respectively, the charts being self explanatory. It has been stated that a more refined antitoxin should be used containing only the globulin fraction. In these cases the antitoxin used was such a preparation; nevertheless the patients had severe chills. Only one patient had a severe reaction with intramuscular injection, two with intraperitoneal, while thirty-five of the thirty-eight

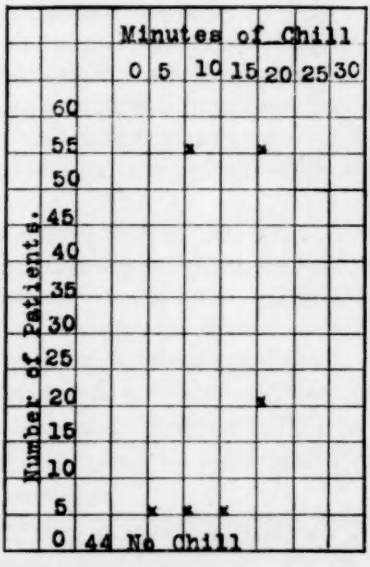

Chart 8.—The number and length of time of chills after intraperitoneal injection. The average length of chills was between fourteen and fifteen minutes. Twelve per cent. of the patients had chills.

patients injected intravenously had reactions that we could classify as severe, five of these patients becoming unconscious for periods of thirty to 120 minutes after the injection.

Intraperitoneal injection would be of no value unless it could be shown that there is a more rapid absorption by the blood stream with this method, as compared with other methods of administration. To quote, Platou:

> The most striking difference in the two methods (referring to intramuscular as compared to intraperitoneal injections) is manifest in the first seven hours, the time of greatest importance. Within an hour after intraperitoneal injection, the blood is appreciably antitoxic, and up to seven hours the absorption is about five times that of the intramuscular.

Clinically also the evidence is in favor of quick absorption by the peritoneum. Membranes disappear in about the same length of time where the intravenous and intraperitoneal injection is used, and the general condition of the patient appears to be better sooner with the two methods just mentioned than with the intramuscular injection.

The intraperitoneal injection was tolerated well in all the cases. One patient with no history of protein sensitivity had a violent reaction, beginning five minutes after the injection and lasting for ten minutes. We believe that this patient would have had just as severe if not a more severe reaction if the antitoxin had been given intravenously. In five patients menstruation was started again. No other effects were noted.

This method of injection is not recommended for all cases of diphtheria, but it seems to be the method of choice in cases of toxic myocarditis where the shock associated with intravenous injection might very well be avoided by intraperitoneal injection, and in infants and children who have had diphtheria for more than two days and who have poor veins.

It is a comparatively safe method, but proper surgical precautions must be practiced before puncturing the peritoneum. We have usually followed Blackfan's [4] technic.

CONCLUSIONS

1. We have compared fifty cases of diphtheria treated by intraperitoneal injection with other methods of antitoxin in administration.

2. We agree with Platou when he states that the method is a safe and simple one.

3. We have shown that antitoxin may be used intraperitoneally, just as it is received from the commercial house, undiluted with saline solution.

4. We believe that this method is the method of choice in severe cases of toxic myocarditis.

Since the foregoing was written, we have injected 118 additional patients, making in all 168 cases of diphtheria treated with antitoxin injected intraperitoneally. The facts gleaned from the additional injections have not changed our conclusions.

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4. Blackfan, Kenneth D., and Maxcy, Kenneth F.: The Intraperitoneal Injection of Saline Solution, Am. J. Dis. Child. **15**:19 (Jan.) 1918.

PROGRESS IN PEDIATRICS

A REVIEW OF THE RECENT LITERATURE ON THE BLOOD*

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Since the review written by Hill [1] in 1922, hundreds of contributions to the literature of the blood have been made. Many of these are of great interest in a physiologic sense; a few are important from the point of view of clinical medicine; most of them add little if anything to our general understanding of the diseases of the blood. Though enough progress has been made in certain chemical problems to permit the formulation of well ordered syntheses, the clinical concepts of diseases of the blood in infants and children remain disorderly and impracticable.

In writing the present review, the object has been to include particularly articles of general physiologic interest and articles having to do with clinical problems in pediatrics. Case reports and descriptions of technical procedures have been alluded to only briefly; not because these are unimportant but because their interest usually lies in details which could not be included without making the report inordinately long. For the sake of clearness, the following plan, not intended as a classification of the blood diseases, has been followed.

1. *Physiologic Considerations.*
    1. The volume and concentration of the blood.
    2. Chemistry of the blood.
        1. Nitrogenous constituents.
        2. Carbohydrate constituents.
        3. Salts, especially calcium and phosphorus.
    3. The Red Cells.
        1. Number, volume and hemoglobin content. Color index and volume index. Physical properties.
        2. Chemistry of the red corpuscles.
            1. The transport of oxygen and carbon dioxid.
            2. Regulation of neutrality.
            3. Regulation of omotic pressure.
        3. The histogenesis and histology of the red cells.
        4. Blood grouping.
    4. The White Cells.
        1. Quantitative considerations.
        2. Histogenesis and functions.
    5. The blood platelets and other elements of the coagulation mechanism.
    6. The spleen and lymph nodes.

* Received for publication, Dec. 30, 1924.

1. Hill, L. W.: A Review of the Literature on the Blood and Blood Diseases of Infants and Children for the Last Four Years, Am. J. Dis. Child. **25**:168 (Feb.) 1923.

2. *Diseases Involving the Hemopoietic System.*
    1. Anemias.
        1. Idiopathic anemias (i. e., well recognized anemias of unknown etiology and not associated constantly with any other recognized disease).
            1. Anemia of the new-born.
            2. Aplastic anemia.
            3. Sickle cell anemia.
            4. Pernicious anemia.
        2. Secondary anemias (i. e., diseases in which anemia is an important feature and in which the cause of the anemia is known or in which the anemia is constantly associated with a well recognized disease or syndrome).
            1. Anemia due to blood loss.
            2. Nutritional anemia.
            3. Anemia due to infection.
            4. Von Jaksch's anemia.
            5. Others.
    2. Polycythemia.
        1. Erythremia.
        2. Functional polyglobulia.
    3. Leukocytosis.
        1. Primary leukocytosis or leukoma: chloroma and myelogenous leukemia.
        2. Functional leukocytosis.
            1. General.
            2. Eosinphilia.
            3. Mononucleosis.
            4. Lymphocytosis.
    4. Disturbances of the coagulation mechanism.
        1. Hemorrhagic disease of the new-born.
        2. Hemophilia.
        3. Purpura.
            1. Thrombopenic purpura.
                1. Primary: Idiopathic purpura hemorrhagica.
                2. Secondary.
            2. Nonthrombopenic purpura.
                1. Primary: Purpura hemorrhagica.
                Purpura simplex.
                Henoch's purpura.
                2. Secondary: Symptomatic purpura.
                Rheumatic purpura.
    5. The use of transfusion in the treatment of anemia and hemorrhagic diseases.
    6. Special blood parasites.
        1. Malaria.
        2. Filariasis hominis sanguinis.
    7. Disturbances of the spleen and lymph nodes.
        1. Primary.
            1. Sarcoma.
            2. Lymphatic leukemia.
            3. Hodgkin's disease.
            4. Gaucher's disease.
            5. Hemolytic jaundice.
        2. Secondary.
            1. Infection.
            2. Cirrhosis of the spleen.
    8. Splenectomy.

PHYSIOLOGIC CONSIDERATIONS

The Volume and Concentration of the Blood.—The investigations of Marriott [2] and of Lucas [3] on the volume of the blood in infants and children have stimulated further work during the last two years. Bakwin [4] and his collaborators have studied especially the concentration of the protein of the blood serum in infants with fever and dehydration, and [5] the volume of the blood in new-born and in marantic infants. These investigators [4] find that marked weight loss in the new-born is usually but not always accompanied by a diminution in skin elasticity and an increase of serum protein concentration, but that the converse does not necessarily hold: the water content of the plasma may increase without increase in weight. Moreover, marked and rapid increase in weight may occur without increase in plasma water content.[6] On the other hand,[5] in new-born infants suffering from dehydration, there is an increased concentration of the serum proteins. With fall in temperature there is a coincidental increase in the water content of the plasma. The administration of water by mouth causes a more rapid and more regular fall in temperature and serum protein concentration than the administrations of water hypodermically or intraperitoneally.[7] In a more recent communication, Bakwin and Rivkin [8] report the results of blood volume determinations in normal infants and in marantic infants. Their results confirm the earlier results of Lucas: the blood volume is generally higher in infants than in adults. They find also a higher total blood volume and especially a higher plasma volume in marantic than in normal infants.

These researches lead, of course, directly to the question of the relation of the blood volume and the protein concentration of the blood to the concentration of the crystalloid constituents of the plasma. This

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2. Marriott, W. M.: Some Phases of the Pathology of Nutrition in Infancy, Harvey Society Lectures, 1920-1921.

3. Lucas, W. P., and Dearing, B. F.: Blood Volume in Infants Estimated by the Vital Dye Method, Am. J. Dis. Child. **21**:96 (Jan.) 1921.

4. Bakwin, H., et al.: Dehydration in New-Borns, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

5. Bakwin, H., et al.: Dehydration Fever in New-Borns, Am. J. Dis. Child. **24**:508 (Dec.) 1922.

6. Bakwin, H.: Oxygen Therapy in Premature Babies with Anoxemia, Am. J. Dis. Child. **25**:157 (Feb.) 1923; The Water Content of Infants' Blood During Rapid Increase of Weight, ibid. **25**:406 (May) 1923.

7. Bakwin, H.; Morris, R. M., and Southworth, J. D.: The effect of Fluid on the Temperature and Blood Concentration in the New-born with Fever, Am. J. Dis. Child. **27**:578 (June) 1924.

8. Bakwin, H., and Rivkin, H.: Estimation of Volume of Blood in Normal Infants and in Infants with Severe Malnutrition, Am. J. Dis. Child. **27**:340 (April) 1924.

phase of the problem has not been investigated in infants, though the work of Norgaard and Gram [9] on the conductivity and freezing point of the plasma in adults points to interesting possibilities.

THE CHEMICAL COMPOSITION OF THE BLOOD

Organic Constituents.—In a chemical study of the blood of mother and fetus, Howe and Givens [10] found no important, constant difference between the concentration of nonprotein nitrogen, uric acid nitrogen and urea nitrogen in maternal and fetal blood, thus confirming the work of previous investigators. Hoeffel and Moriarty,[11] using the new method of Folin and Wu [12] for the determination of the amino-acid nitrogen of the blood, found an average value of 5.42 mg. of amino-acid nitrogen per hundred cubic centimeters of blood in the normal infant and child. The level of amino-acid nitrogen was found to bear no relation to the age of the infant or child but was slightly lower than the adult mean value 4 mg. Using the revised uric acid method of Folin,[13] these investigators found a mean uric acid value for infants and children of 3.45 mg. per hundred cubic centimeters of blood, as opposed to the mean normal adult value of 4.05 mg. The individual variations from the mean were greater in infants and in children (from 2.56 to 5.88) than in adults (from 3.78 to 4.75). The values for the nonprotein nitrogen content of the blood of infants and children do not differ essentially from the values for normal adults.

Leopold, Bernhard and Jacobi,[14] in a study of the uric acid metabolism on various diets, found that neither the administration of uric acid nor various changes in the diet would influence the level of the nonprotein nitrogenous constituents, or the sugar, of the blood. They used Benedict's method [15] and their values for uric acid in the blood are thus lower, usually under 3 mg., than those found by other workers who used Folin's method.

Difficulties in the determination of uric acid in the blood continue to appear in reports in the literature. Though different methods

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9. Norgaard, A., and Gram, H. C.: Chlorid and Conductivity Determinations on Plasma, J. Biol. Chem. **56**:429 (June) 1923.

10. Howe, M. G., and Givens, M. H.: Chemical Studies of the Blood of Mother and Fetus, Am. J. Dis. Child. **25**:63 (Jan.) 1923.

11. Hoeffel, G. N., and Moriarty, M. E.: Amino-Acid Content of Blood of Infants and Children, Am. J. Dis. Child. **27**:64 (Jan.) 1924.

12. Folin, O., and Wu, H.: System of Blood Analysis; New Colorimetric Method for Determination of Amino-Acid Nitrogen in Blood, J. Biol. Chem. **51**:377 (April) 1922.

13. Folin, O.: System of Analysis: Revision of Uric Acid Method, J. Biol. Chem. **54**:153 (Oct.) 1922.

14. Leopold, J. S.; Bernhard, A., and Jacobi, H. G.: Uric Acid Metabolism of Children, Am. J. Dis. Child. **27**:243 (March) 1924.

15. Benedict, S. R.: Determination of Uric Acid in Blood, J. Biol. Chem. **51**:187 (March) 1922.

yield results consistent within themselves, the results differ according to the methods used. Recently, Morris and MacLeod [16] have reported a method for the determinaion of a "Second Form" of uric acid not included in the determination by the Folin method. According to Morris and MacLeod, the total amount of uric acid in the blood is somewhat higher than previously suspected, certainly very much higher than the 1 to 2 mg. per hundred cubic centimeters originally found by Folin.

A new technic, based on the Folin-Wu method, for estimating the sugar content of small amounts of blood has been described by Kramer [17] and this procedure should be of service to pediatricians. It is to be noted, however, as pointed out by Foster [18] and others, that capillary blood is richer in sugar than venous blood and that its content of sugar stands between that of arterial and that of venous blood during the period following the ingestion of sugar. On the other hand, in the fasting individual the three types of blood contain essentially the same quantity of sugar. Hence, in determining the sugar tolerance of a person it must be borne in mind that estimations based on capillary blood are not comparable to those obtained from the use of venous blood.

Inorganic Constituents.—During recent years, numerous investigations have had to do with studies of the phosphorus and calcium of the blood. As these researches have been concerned principally with rickets and tetany and are thus reported by other reviewers, they will not be discussed in detail in this paper. The reader is referred especially to the comprehensive reviews published by Park,[19] by Howland [20] and by MacCallum.[21]

Since the publication of the work of Howland and Marriott,[22] demonstrating a diminished calcium content of the blood in active tetany, and particularly since the investigations of Kramer and How-

16. Morris, J. L., and MacLeod, A. G.: Colorimetric Determination of Uric Acid, Estimation of 0.03 to 0.5 Mg. Quantities by New Method, J. Biol. Chem. **50**:55 (Jan.) 1922.

17. Kramer, B., and Gittleman, I. F.: Technic for Quantitative Estimation of Sugar in Very Small Amounts of Blood, J. A. M. A. **81**:1171 (Oct. 6) 1923.

18. Foster, G. L.: Carbohydrate Metabolism: Some Comparisons of Blood Sugar Concentration in Venous and Capillary Blood, J. Biol. Chem. **55**:291 (Feb.) 1923.

19. Park, E. A.: Etiology of Rickets, Physiol. Rev. **3**:106 (Jan.) 1923.

20. Howland, J.: Etiology and Pathogenesis of Rickets, Medicine **2**:349 (Nov.) 1923.

21. MacCallum, W. G.: Pathogenesis of Tetany, Medicine **3**:137, 1924.

22. Howland, J., and Marriott, W. M.: Observations Upon the Calcium Content of the Blood in Infantile Tetany and Upon the Effect of Treatment by Calcium, Quart. J. Med. **11**:289 (July) 1918.

land [23] and those of Kramer, Howland and Tisdall [24] on the calcium and phosphorus contents of the blood of normal and rachitic infants, many observations have been reported concerning the factors which might influence the concentration of these constituents of the blood. A. F. Hess and Lundagen [25] have shown that a seasonal variation in the phosphorus content of blood serum occurs: the serum is normally richer in phosphorus in summer and fall than in winter and spring. Tisdall and Harris [26] have shown that the phosphorus content of the blood serum is increased in persons with healing bone fractures, and Eddy and Heft [27] report a similar rise in phosphorus content in patients with granulating wounds.

The influence of infectious disease on the level of the blood phosphorus is brought out by the work of Gerstenberger, Burhans, Smith and Wetzel.[28] According to these authors, there is a diminution in the inorganic phosphorus of the blood in infants who, though showing no signs of rickets, suffer from pneumonia. In some cases the quantity of calcium is also reduced. When recovery takes place, the phosphorus and calcium return to normal levels.

A. F. Hess and Matzner [29] found that the inorganic phosphorus content of the blood of the new-born is usually lower than that of infants 1 month of age or older, but they were unable to demonstrate rickets in any case even though the quantity of phosphorus was markedly below normal. Moreover, there was no relationship between the quantity of phosphorus in the blood of the new-born and the occurrence of rickets in the first year of life. The quantity of inorganic phosphorus in maternal blood was almost always less than in the blood of the new-born.

Concerning the relationship between phosphorus and calcium in the blood in rickets, it is pointed out by Kramer and Howland [30] that

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23. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

24. Kramer, B.; Howland, J., and Tisdall, F. F.: The Clinical Significance of Calcium Concentration in the Serum of Children and Possible Errors in Its Determination, Am. J. Dis. Child. **22**:560 (Dec.) 1921.

25. Hess, A. F., and Lundagen, M. A.: A Seasonal Tide of Blood Phosphate in Infants, J. A. M. A. **79**:2210 (Dec. 30) 1922.

26. Tisdall, F. F., and Harris, R. I.: Calcium and Phosphorus Metabolism in Patients with Fractures, J. A. M. A. **79**:884 (Sept. 9) 1922.

27. Eddy, W. H., and Heft, H. L.: The Relation of Fracture Healing to the Inorganic Phosphorus of the Blood Serum, J. Biol. Chem. **55**:12, 1923.

28. Gerstenberger, H. J.; Burhans, C. W.; Smith, D. N., and Wetzel, N. C.: The Blood Serum Content of Inorganic Phosphorus and Calcium in Pneumonia, Am. J. Dis. Child. **26**:329 (Oct.) 1923.

29. Hess, A. F., and Matzner, M. J.: Rickets in Relation to Inorganic Phosphate and Calcium in Maternal and Fetal Blood, Am. J. Dis. Child. **26**:285 (Sept.) 1923.

30. Kramer, B., and Howland, J.: Factors Which Determine Concentration of Calcium and of Inorganic Phosphorus in Blood Serum of Rats, Bull. Johns Hopkins Hosp. **33**:313 (Sept.) 1922.

rickets does not occur provided the product of the calcium and phosphorus contents is greater than 40. If this product is less than 40 but over 30, healing of rickets may occur but normal bone formation cannot take place if the product is less than 30.

According to Hess and his co-workers,[31] the phosphorus content of the blood is always reduced in severe rickets, though the calcium content of the blood may be normal. On the other hand, in cases of tetany accompanied by rickets, the calcium content of the blood is always reduced, though the phosphorus content may not be markedly abnormal. In cases of severe rickets accompanied by tetany under treatment, the blood phosphorus shows a tendency to remain stationary or to diminish until the calcium has reached a normal level.

The influence of cod liver oil and of ultraviolet radiation on the calcium and phosphorus levels of the blood in rickets and tetany has recently received much study. Park, Guy and Powers [32] have brought forth proof of the regulatory influence of cod liver oil. Tisdall [33] and Kramer, Casparis and Howland [34] have shown the beneficial effect of ultraviolet rays on the calcium and phosphorus contents of the blood in cases of rickets, and Hoag [35] has demonstrated the efficacy of this type of treatment in elevating the calcium content of the blood in tetany.

The mode of action of hydrochloric acid producing substances (calcium chlorid, ammonium chlorid, hydrochloric acid) in the treatment of tetany has been investigated by Gamble and Ross.[36] It is the diminution in the concentration of calcium ions rather than in the concentration of total calcium in the blood plasma that permits the development of tetany. The former is dependent on the ratio of hydrogen-ion concentration to bicarbonate-ion concentration in the

31. Hess, A. F.; Calvin, J. K.; Wang, C. C., and Felcher, A.: Calcium and Phosphorus Determinations in the Blood Plasma in Rickets and Tetany, Am. J. Dis. Child. **26**:271 (Sept.) 1923.

32. Park, E. A.; Guy, R. A., and Powers, G. F.: A Proof of the Regulatory Influence of Cod Liver Oil on Calcium and Phosphorus Metabolism, Am. J. Dis. Child. **26**:103 (Aug.) 1923.

33. Tisdall, F. F.: Effects of Ultraviolet Rays on Calcium and Inorganic Phosphate Content of Blood Serum of Rachitic Infants, Canad. M. A. J. **12**:536 (Aug.) 1922.

34. Kramer, B.; Casparis, H., and Howland, J.: Ultraviolet Radiation in Rickets. Effect on the Calcium and Inorganic Phosphorus Concentration of the Serum, Am. J. Dis. Child. **24**:20 (July) 1922.

35. Hoag, L. A.: The Treatment of Infantile Tetany with Ultraviolet Radiation: Its Effects on the Clinical Symptoms and on the Calcium Concentration in the Blood Serum, Am. J. Dis. Child. **26**:186 (Aug.) 1923.

36. Gamble, J. L., and Ross, G. S.: Studies of Tetany. II. The Effect of Ingestion of Hydrochloric Acid Producing Substances on Acid-Base Metabolism of an Infant and the Probable Manner of Their Action in the Treatment of Tetany, Am. J. Dis. Child. **25**:470 (June) 1923.

plasma, and can be calculated from Michaelis'[37] modification of the formula of Rona and Takahaski: $[Ca^{++}] = 340 \times \frac{[H^+]}{[HCO_3]}$ moles per liter. Gamble, Ross and Tisdall[38] have shown that ammonium chlorid, calcium chlorid and hydrochloric acid act similarly in that they permit the elevation of the level of chlorid ion at the expense of bicarbonate ion in the plasma, the total base remaining constant. The hydrogen-ion concentration is thus increased at the same time that the bicarbonate-ion concentration is depressed and, according to the foregoing equation, the calcium-ion concentration is also increased.

In considering the literature of blood phosphorus in its relation to rickets and tetany, due mention should be made of the very interesting work of Robison, Soames and Kay.[39] These workers have shown that in the ossifying cartilage and teeth of young animals, especially in rachitic animals, there is an esterase capable of hydrolyzing, in part, the hexosephosphoric esters of the blood.

These esters are present almost entirely in the corpuscles which act as reservoirs and from which they diffuse into the plasma. The optimum p_H for the action of the esterase lies on a plateau, extending from a value of 8.4 to a value of 9.4, a range which is favorable also for the precipitation of calcium phosphate. Though attention has hitherto been directed almost exclusively to the inorganic phosphoric acid, it may turn out to be true that the lowered phosphorus content of the blood plasma of rachitic persons is a result of an insufficient supply of phosphoric acid ester and not the primary cause of the failure of the deposition of calcium phosphate.

THE CHEMISTRY OF HEMOGLOBIN

In recent years, the physical chemistry of hemoglobin has attracted increasing attention. It has long been an "open secret" that the diminution of the carbon dioxid tension in the lungs is not a satisfactory explanation of the evacuation of carbon dioxid from the blood. This phenomenon has at last been elucidated by the work of Hender-

37. Michaelis, L., quoted by Gamble and Ross: Die Wasserstoffionenkonzentration, Berlin **1**:71, 1922.

38. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: Studies of Tetany. I. The Effect of Calcium Chlorid Ingestion on the Acid-Base Metabolism of Infants, Am. J. Dis. Child. **25**:455 (June) 1923.

39. Robison, R.; Soames, K. M., and Kay, H. D.: A New Phosphoric Ester Produced by the Action of Yeast Juice on Hexosis, Biochem. J. **16**:809, 1922; The Possible Significance of Hexose-Phosphoric Esters in Ossification, ibid. **18**:740, 1924; The Possible Significance of Hexose-Phosphoric Esters in Ossification, ibid. **18**:755, 1924.

son,[40] who has shown that as the hemoglobin becomes oxygenated it becomes sufficiently acid to liberate carbon dioxid from its combination with base, the latter then combining with hemoglobin. The reverse change takes place in the tissues, where the increased tension of carbon dioxid is sufficient to drive off the oxygen from the blood, thus liberating base for combination with carbon dioxid.

But the red corpuscles do more than carry all of the bound oxygen and part of the carbonic acid. Henderson and Haggard [41] have shown that the red corpuscles are capable of manufacturing bicarbonate when placed in a solution of sodium chlorid. They thus become an important part of the neutrality regulating mechanism of the blood. As the carbon dioxid tension to which the blood is exposed increases, more bicarbonate is formed, so that the ratio between combined and dissolved carbonic acid in the blood may be maintained constant within wide limits of carbon dioxid tension. Beyond these limits the p_H may change (uncompensated acidosis). This subject of neutrality regulation has been reviewed at length by Wilson.[42]

It has long been known that with increasing carbon dioxid tension, chlorid ions pass from plasma to corpuscles, coincidentally with an increased bicarbonate content of the plasma. The phenomenon has never been satisfactorily explained, though it has been suggested by Buckman and Edwards [43] that free amino groups in the corpuscles may permit the formation of sodium bicarbonate and aminohydrochlorid from sodium chlorid and carbonic acid, according to a reaction analogous to that which occurs in the formation of sodium bicarbonate in the Solvay process, thus:

$$R\text{–}N\ H_2 + NaCl + H_2\ CO_3 = NaHCO_3 + R\text{–}N\ H_2\ H\ Cl.$$

Hydrochloric acid enters the corpuscles and the plasma gains sodium bicarbonate, molecule for molecule, in place of sodium chlorid. As sodium bicarbonate and sodium chlorid are about equally dissociated, there is no important net change in the number of particles in the plasma. The cells, however, suffer an increase in concentration of particles, and water flows in to restore the equilibrium, thus concentrating the plasma; a phenomenon demonstrated by Kovács [44] and studied

40. Henderson, L. J.: The Equilibrium Between Oxygen and Carbonic Acid in Blood, J. Biol. Chem. **41**:401 (March) 1920.

41. Henderson, Y., and Haggard, H. W.: Hemato-Respiratory Functions, J. Biol. Chem. **45**:189 (Dec.) 1920.

42. Wilson, D. W.: Neutrality Regulations in the Body, Physiol. Rev. **3**:295 (July) 1923.

43. Buckman, T. E., and Edwards, H. T.: The Mechanism of Chlorid Ion Transferred from Plasma to Corpuscles with Increasing Carbon Dioxid tension, Trans. Am. Soc. Clinical Investigation, 1922, p. 32.

44. Kovács, Josef: Experimentelle Beitrage über die Wirkung von Sauerstoffiinhalation, Berl. klin. Wchnschr. **39**:362, 1912.

by Henderson and Spiro.[45] But as a result of the concentration of the plasma, water must flow from the tissues into the blood on the venous side of the capillary meshwork. This process, depending on the difference between the tensions of carbon dioxid to which arterial and venous blood are exposed, may have an important bearing on the resorption of water from the tissues.

Lundsgaard and Van Slyke [46] have studied the factors which determine cyanosis and the degree of unsaturation of the blood with oxygen. Their comprehensive monograph should be consulted by any one interested in this subject.

The interrelations of oxygen and carbon dioxid tensions, of oxygen and carbon dioxid contents of the blood, of the hydrogen-ion concentration of the plasma and of the transference of salts at different tensions of carbon dioxid have been clearly set forth by Henderson, Bock, Field and Stoddard.[47] The removal of carbon dioxid from the body, the delivery of oxygen to the tissues, the regulations of the neutrality of the blood plasma and probably also the regulation of the osmotic pressure of the plasma and the transfusion of water across the capillaries, are all quantitatively related and the relationships can be expressed systematically by means of a nomogram or alignment diagram.

The difficulty, if not the impossibility, of securing arterial blood from infants and children makes the study of the cycle of changes almost impossible in early life, though much might be learned from a study of carbon dioxid dissociation curves and the venous blood alone.

BLOOD HISTOLOGY

Because of their great general interest, attention is called to the excellent review of Sabine [48] on the origin of the cells of the blood, to that of Rous [49] on blood destruction in health and disease and to the one by Bunting [50] on the leukocytes.

Of special interest also is the work of Drinker, Drinker and Lund [51] on the factors that govern the delivery of red corpuscles to the circulation. These investigators have demonstrated that the rate at which

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45. Henderson, L. J., and Spiro, K.: Biochem. Ztschr. **15**:114, 1908.
46. Lundsgaard, C., and Van Slyke, D. D.: Cyanosis, Medicine **2**:1 (Feb.) 1923.
47. Henderson, L. J.; Bock, A. V.; Field, H., Jr., and Stoddard, J. L.: Blood as a Physicochemical System, J. Biol. Chem. **59**:379 (March) 1924.
48. Sabine, F. R.: Origin of the Cells of the Blood, Physiol. Rev. **2**:38 (Jan.) 1922.
49. Rous, P.: Destruction of Blood Corpuscles in Health and Disease, Physiol. Rev. **3**:75 (Jan.) 1923.
50. Bunting, C. H.: The Leukocytes, Physiol. Rev. **2**:505 (Oct.) 1922.
51. Drinker, K. R.; Drinker, C. K., and Lund, C. C.: Circulation in the Mammalian Bone Marrow, Am. J. Physiol. **62**:1 (Sept.) 1922.

red cells are delivered to the marrow capillaries is governed by the difference between growth pressure within the marrow and the pressure within the capillaries. Whenever any influence, such as hemorrhage, causes an increased proliferation of red cells, the growth pressure increases and more red cells are temporarily delivered to the circulation. Immature forms, which are found toward the center of the islands of proliferating red cells, ordinarily are not thrown into the circulation because of their adhesiveness, but under abnormal stimulation they may be forced out prematurely into the capillaries. As the stimulus subsides, the normal rate of delivery is resumed. The process presumably occurs more readily in young persons, and may in certain instances explain why immature red cells so frequently appear in infantile blood. Yet it is difficult to understand why, in infections, for example, there should so frequently be an outpouring of young red cells, as infection is not ordinarily considered a stimulus to red cell proliferation.

Ashby [52] has introduced an ingenious method for studying the length of life of red corpuscles by transfusing red cells of a different but compatible group into patients, and then making daily counts of the number of cells which can be agglutinated. According to this method, Ashby finds the length of life of transfused red cells to be about three months in pernicious anemia, though Wearn, Warren and Ames [53] found a maximum life span of from fifty-three to 113 days in the case of cells transfused into patients suffering from pernicious anemia and chronic nephritis. On the other hand, Isaacs [54] believes, from his own experiments, that transfused red cells do not persist in the circulation for more than from four to five days. The question remains open.

The mode of destruction of red cells seems still to be a much mooted question. The work of Rous [55] points to some process of attrition or wearing down of the red corpuscles, or possibly to partial hemolysis, preceding phagocytosis by endothelial cells. On the other hand, it is contended by some that phagocytosis is almost entirely responsible for red cell destruction. It is, however, difficult to put aside the histologic evidence that humoral factors are at work in red cell destruction, at least in those conditions in which presumably an increased destruction

52. Ashby, F.: Study of Transfused Blood, J. Exper. Med. **29**:267, 1919; ibid. **34**:147 (Aug.) 1921.

53. Wearn, J. T.; Warren, S., and Ames, A.: The Length of Life of Transfused Erythrocytes in Patients with Primary and Secondary Anemia, Arch. Int. Med. **29**:52 (April) 1922.

54. Isaacs, R.: The Effects of Hemorrhage, Transfusion and Irradiation on the Production and Maturation of Red Blood Cells, J. A. M. A. **82**:2078 (June 21) 1924.

55. Rous, P.: Footnote 49.

of blood occurs. Moreover, Buckman and Horrall [56] have shown that normal red cells are less resistant to hypotonic serum from cases of hemolytic anemia than to normal serum of the same iso-agglutination group, and Clark, Evans and Zinck [57] have shown that red cells of the rat are more resistant to hemolysis caused by sodium oleate when mixed with normal serum than when mixed with the serum of a patient suffering from pernicious anemia. These findings would indicate that the blood serum might well influence the rate of destruction of red blood corpuscles.

BLOOD GROUPING

Guthrie and Huck [58] have demonstrated by direct tests and by absorption experiments the existence of a third iso-agglutinin and a third iso-agglutinogen in human blood, thus making twenty-seven possible biologic combinations. The practical application of these findings to problems of transfusion in infancy is not now evident, but it does make the problem of determining legitimacy of offspring on the basis of blood grouping more difficult.

Ottenberg [59] has published investigations tending to support von Dungern and Hirschfeld's conception of the hereditary nature of the blood groups and their medicolegal application. Further work on this subject has been done by McQuarrie,[60] by Dyke [61] and by Dyke and Budge.[62] The investigations of the latter authors seem to substantiate further the conception of von Dungern and Hirschfeld that it is not the actual blood groups but the agglutinogens which are inherited. On the other hand, Buchanan [63] points out that the generalizations of Ottenberg, relative to inheritance of blood groups, may not hold in a given case owing to the possibility, always present, of a heterozygous grandparent,

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56. Buckman, T. E., and Horrall, O. H.: Types of Purpura in Infants and Children, M. Clin. N. Am. **5**:1441 (March) 1922.

57. Clark, H. M.; Evans, F. A., and Zinck, R. H.: Resistance of Red Cells to Sodium Oleate, Bull. Johns Hopkins Hosp. **33**:16 (Jan.) 1922.

58. Guthrie, C. G., and Huck, J. G.: Existence of More than Four Iso-agglutinin Groups in Human Blood, Bull. Johns Hopkins Hosp. **34**:37 (Feb.) 1923; ibid. **34**:80 (March) 1923; ibid. **34**:128 (April) 1923.

59. Ottenberg, R.: Medicolegal Application of Human Blood Grouping, J. A. M. A. **78**:873 (March 25) 1922.

60. McQuarrie, I.: Iso-Agglutination in New-Born Infants and Their Mothers, Bull. Johns Hopkins Hosp. **34**:51 (Feb.) 1923.

61. Dyke, S. C.: On Medicolegal Importance of the Blood Groups, Lancet **2**:1271 (Dec. 16) 1922.

62. Dyke, S. C., and Budge, C. H.: On the Inheritance of Specific Iso-agglutinable Substances of the Human Red Cells, Proc. Roy. Soc. Med. (Sect. Path.) **16**:35 (May) 1923.

63. Buchanan, J. A.: Medicolegal Application of the Blood Group, J. A. M. A. **78**:89 (Jan. 14) 1922; Am. J. M. Sc. **165**:675, 1923.

and he cites cases to prove his point. Certainly in the present state of our knowledge, it would seem hazardous to depend on blood grouping as a means of determining legitimacy.

For the same reason, in contemplating the transfusion of an infant, it is not fair to assume that the blood of a parent is necessarily compatible with that of the offspring. That hemolytic reactions are rare in infants who have been given a transfusion of blood from a parent, the compatibility of which has not been determined, is due probably to the usually but not invariably low concentration of agglutinins in infants' serum.

THE NUMBERS OF BLOOD CORPUSCLES

The work of Williamson [64] on the hemoglobin content of the blood, and the more recent work of Mayers [65] on the number of red cells in the blood of normal persons of different ages, have provided standards of comparison for the study of these important factors.

Lippman [66] has made an exhaustive statistical study of the blood histology of seventy-one normal infants during the first five days of life. Estimations of the numbers of corpuscles and study of their morphology were made at very frequent intervals, thus permitting accurate delineation of the fluctuations in the levels of the various types of blood cells. The more important conclusions are here summarized:

1. The red blood cells at birth average 5.2 millions per cubic millimeter. During the first six hours the count rises to 5.6 millions. Following this there is a drop to 5.4 millions at eighteen hours, after which time the count remains fairly constant until forty-eight hours after birth.

2. The platelet count at birth average 213,000 per cubic millimeter. It drops to 170,000 during the first six hours. The decrease continues until eighteen hours after birth and is then followed by a slight increase. No changes from normal were observed in the platelet counts in icterus neonatorum.

3. The total leukocyte count at birth averages 16,000 per cubic millimeter. At twelve hours it is 22,500, after which it gradually drops to 11,300 at forty-eight hours. At five days it has decreased to 9,500.

4. The differential counts of the leukocytes show very wide variations. The polymorphonuclear leukocyte count, in absolute numbers, follows closely the total leukocyte count in early life. Neutrophilic metamyelocytes are numerous in the blood during the new-born period but younger myelogenous cells are unusual.

5. The absolute values of the lymphocytes vary little during the first five days. At birth and six hours after they are most numerous. There is a slight drop at twelve hours, followed by a fairly constant number until forty-eight

64. Williamson, C. S.: Influence of Age and Sex on Hemoglobin. A Spectrophotometric Analysis of Nine Hundred and Nineteen Cases, Arch. Int. Med. **18**:505 (Oct.) 1916.

65. Mayers, L. H.: A Study of the Erythrocyte Curve at Various Ages and Its Relationship to the Hemoglobin Curve, Arch. Int. Med. **30**:478 (Oct.) 1922.

66. Lippman, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

hours after birth. Between forty-eight hours and five days after birth there is a slight increase. The curves taken by the small, medium and large lymphocytes are quite similar to the curve of the total lymphocytes.

6. The relative and absolute values of lymphocytes and neutrophils are equal at forty-eight hours. After this time the values for the lymphocytes increase while those for the neutrophils decrease.

7. Mononuclear and transitional cells were found to be present in the same percentages as in later life. The eosinophils were found gradually to rise in number until thirty-six hours after birth and then to become less numerous. Basophiles (mast cells) were found to be rare. The numbers of degenerated leukocytes followed the total white count in a general way.

8. The study of the red corpuscles revealed the presence of nucleated forms in every case at birth (?), in one-half the cases at forty-eight hours and in only one case at five days. Basophilic stippling was not observed but polychromasia was always present. Anisocytosis was generally observed and poikilocytosis was often present. Rouleaux formation was less frequently observed than in normal adult blood.

9. Mathematical analysis of the data showed marked differences in the variability of the different elements from the average. The red cell count was least variable, its average variability being about eleven per cent. The variability of the platelet count was great at all times. The average variability of the total leukocyte count was about 25 per cent., of the total polymorphonuclear neutrophil count about 35 per cent., and of the total lymphocyte count about the same.

The author is of the opinion that the observed changes cannot be accounted for on the basis of increased blood concentration, but rather that the increased numbers of red corpuscles and white corpuscles, together with the presence of immature and atypical forms, constitute evidence in favor of increased activity on the part of hemopoietic organs. One is surprised to find, however, that the platelets do not share in the process, as they are so often increased in conditions associated with increased bone marrow activity.

Drucker [67] has studied the relationship between the percentage by volume of red corpuscles and their hemoglobin content in a series of eighty-five healthy infants, aged from 2 weeks to 2 years. He finds that the blood of normal infants has a low color index, this being lowest at about 9 months of age at about which time the cell volume (volume index) also is lowest. From tables which he has compiled, it is possible to detect deviations from standard normal values.

Bakwin and Morris [68] have studied the level of the leukocytes in new-born infants suffering from dehydration fever. They find no increase in the physiologic leukocytosis in this condition.

Considerable interest has attached to the reported influence of germanium dioxid in stimulating the output of red cells from the bone

67. Drucker, P.: Hemoglobin and Corpuscle Volume in Infants, Hospitalstid. **66**:110 (Feb. 7) 1923.

68. Bakwin, H., and Morris, R. M.: Leukocyte Count in the New-Born with Dehydration Fever, Am. J. Dis. Child. **26**:23 (July) 1923.

marrow. Hammett, Nowrey and Müller [69] have reported marked increase in the red cell count within a week following the intravenous injection of a solution of germanium dioxid in rats, and similar results have been reported by Müller and Iszard [70] and others. The work of Minot and Sampson [71] shows fairly definitely, however, that so far as adult human beings are concerned, no particular influence is exerted by germanium dioxid in stimulating the production of red cells.

COAGULATION MECHANISM

Very careful studies of the variations in the blood platelets in the new-born have been reported by Lippman.[66] He found an average of 213,000 per cubic millimeter at birth, followed by a decrease during the following eighteen hours and then a rise. No changes were observed in icterus neonatorum. Emmanuele [72] obtained substantially the same results, and observed also that premature infants have a somewhat greater number of platelets than normal infants at birth. According to Emmanuele the coagulation time of premature infants is shorter than that of normal infants at birth. The coagulation time lengthens slightly with each day of life up to about ten days.

Sherman and Lohnes,[73] in studying a series of 100 infants, found twenty-eight in which the bleeding time was longer than five minutes and twelve in which the coagulation time was longer than twelve minutes. In only one infant did cerebral hemorrhage occur.

Very interesting is the work of Foster and Whipple [74] on the influence of tissue injury on the fibrinogen production. These investigators are of the opinion that the liver is the principal source of fibrinogen. Their experiments indicate that injury to tissue from whatever cause stimulates fibrinogen production. The evidence favoring the liver as the principal site of fibrinogen production is especially pertinent, as it may have an important bearing on the pathogenesis of anaphylactic purpura.

Concerning agents devised to shorten the coagulation time of the blood when that has been abnormally prolonged, one notes especially the

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69. Hammett, F. S.; Nowrey, J. E., Jr., and Müller, J. H.: The Erythropoietic Action of Germanium Dioxid, J. Exper. Med. **35**:173 (Feb.) 1922.

70. Müller, J. H., and Iszard, M. S.: Erythropoietic Action. Cumulative Effect and Elimination of Germanium Dioxid, Am. J. M. Sc. **163**:364 (March) 1922.

71. Minot, G. R., and Sampson, J. J.: Germanium Dioxid as a Remedy for Anemia, Boston M. & S. J. **189**:629 (Nov. 1) 1923.

72. Emmanuele, A.: Richerche sulle piastrine e sulla coagulatilita del sangue nel neonato, Pediatria **31**:422, 1923.

73. Sherman, DeW. H., and Lohnes, H. R.: Bleeding and Coagulation in the First Week of Life, N. Y. State J. Med. **23**:146 (April) 1923.

74. Foster, D. P., and Whipple, G. H.: Fibrin Values Affected by Tissue Injury, Am. J. Physiol. **58**:393 (Jan.) 1922.

work of Neuhof and Hirshfeld,[75] who have demonstrated a marked diminution in the coagulation time of the blood following the parenteral administration of sodium citrate. The effect is said to be most marked in cases of jaundice showing a prolonged coagulation time. It is most marked for two to three hours after treatment but some diminution in coagulation time may be noted for as long as forty-eight hours. The authors state that this diminution in the coagulation time does not occur in diseases characterized by platelet defects.

Mills [76] has obtained a tissue fibrinogen from the lungs of animals, which appears to have a marked effect on the coagulation of the blood, causing rapid clotting in vitro but dangerous to administer intravenously on account of the possibilities of intravascular clotting. If this substance can be so prepared as to render its administration by mouth effective, it should be of great potential value in the control of hemorrhage in cases of jaundice due to liver injury.

Much interest has been shown in the possible influence of irradiation therapy, especially by short wave length roentgen rays, on the coagulability of the blood. Fulle [77] reports that irradiating the liver, long bones and especially the spleen will appreciably shorten the coagulation time of the blood. Similar effects have been reported by Schichida [78] and by Zweifel.[79]

PHYSIOLOGY OF THE SPLEEN

Hautman [80] described experiments on animals in which arterial and venous blood from the spleen were studied without removal of the organ. He claims to have demonstrated a destructive action of the spleen on the red cells.

Krumbhaar and Musser [81] have studied extensively the influence of splenectomy on the hemopoietic system. They again point out that one of the most important effects of splenectomy is the increased resistance of the red corpuscles. Their experiments indicate that the post-

75. Neuhof, H., and Hirshfeld, S.: The Intramuscular Administration of Sodium Citrate; a New Method for the Control of Bleeding, Ann. Surg. **76**:1 (July) 1922.

76. Mills, C. A.: Blood Clotting and the Control of Hemorrhage, M. Rec. **101**:149 (Jan. 28) 1922.

77. Fulle, C.: L'irradiazione della milza, fegato, midollo osseo a scope emostatico, Ann. Ital. di Chir. **3**:299, 1913.

78. Schichida: Experimental Study and Clinical Observation on Blood Coagulation, Japan M. World **7**:208, 1922.

79. Zweifel, E.: Zur Frage der Milzreitzertralung, München. Med. Wchnschr. **70**:670 (May 25) 1923.

80. Hautman, H.: Experimentelle Untersuchungen über die Funktion der Milz, Deutsch. med. Wchnschr. **48**:1509, 1922.

81. Krumbhaar, E. B., and Musser, J. H., Jr.: The Effect of Splenectomy on the Hemopoietic System of Macacus Rhesus, Arch. Int. Med. **31**:686 (May) 1923.

splenectomy anemia observed in animals, in this case, monkeys, is due to the disappearance of the bone marrow stimulant normally produced in the spleen. Later, the Kupfer cells in the liver and the lymph nodes seem to take on some of the functions of the spleen, especially stimulation of the bone marrow and red cell destruction.

Further evidence concerning what has been called the hemocatonistic influence of the spleen is brought forth by Bolt and Heeres,[82] whose experiments indicate that in the spleen the red cells are prepared for destruction by alterations in their surface layer, a change which increases their fragility. Other investigations recently reported in the literature concerning the physiology of the spleen are also referred to.[83]

ANEMIAS

Attention is called to the interesting classification of blood diseases in childhood, proposed by Ward.[84] The classification is essentially anatomic, the diseases for the most part being divided into three main groups: those involving all parts of the hematopoietic system, those involving the plasma and those involving the corpuscles. While, in the main, the classification is based on the generally accepted conceptions of diseases of the blood, one is somewhat surprised to find chlorosis and hemophilia associated as diseases involving particularly the plasma.

Donnally [85] reports a case of severe anemia in a new-born infant, and states that the report of only one similar case was found in the literature. Donnally's patient showed histologic evidence of blood regeneration and no evidence of increased blood destruction. No cause for the condition could be found. The infant recovered, following two transfusions of blood. A case showing a somewhat similar blood picture, but in an infant aged 3½ months, is reported by Stransky.[86] Stransky's patient, however, showed evidence of infection at necropsy, and though an instance of severe anemia in a young infant, it is hardly comparable with the case of Donnally.

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82. Bolt, N. A., and Heeres, P. A.: Over des invloed der milt op de roode blood lichampjes, Nederlandsch. Tijdschr. v. Geneesk. **2**:2259 (Nov. 18) 1922.

83. Massaglia, A. C.: The Physiopathology of the Spleen, Journal-Lancet **43**:181 (April 15) 1923; Rosenthal, S. M.: The Rôle of the Liver in the Removal of Hemoglobin from the Blood Stream, J. Pharmacol. & Exper. Therap. **21**:367, 1913; Spadolini, I.: Sulla distruzione fisiologica degli entrocite studiata col metodo delle incezioni vitali di fleu di metilene, Arch. di fisiol. **20**:129, 1922; Voorhoeve, H. C.: Over de outleding van roode bloedlichampjes in de milt, Nederlandsch. Tijdschr. v. Geneesk. **2**:335 (July 28) 1923.

84. Ward, G.: The Classification of Blood Diseases in Childhood, Brit. J. Child. Dis. **20**:84 (April-June) 1923.

85. Donnally, H. H.: Anemia in the New-Born, Am. J. Dis. Child. **27**:369 (April) 1924.

86. Stransky, E.: Clinical Hematology of Infants, Ztschr. f. Kinderh. **35**:195 (April) 1923.

PRIMARY ANEMIAS

Cases of aplastic anemia in children are reported by Herrman [87] and by Spak.[88] Hummel [89] reports a case of fatal anemia in a boy, aged 12, in which the blood picture was consistent with that usually seen in aplastic anemia but in which the bone marrow at necropsy was definitely hyperplastic.

Detailed reports of cases of sickle cell anemia are given by Huck [90] and by Sydenstricker.[91] According to Huck, this disease occurs exclusively in negroes and apparently is inherited according to the mendelian law. Sydenstricker, Mulherin and Houseal [92] report in detail two cases of sickle cell anemia in two negro children.

Hatz [93] reports a case of pernicious anemia in a girl, aged 10 years, and Wischer [94] reports a similar case in a girl, 4½ years of age.

SECONDARY ANEMIAS

Lucas and Hoobler [95] report a series of cases of acutely developing secondary anemias in infants. The cases are grouped into four classes: those in which the anemia is due to mechanical blood loss; those in which the anemia is due to a deficiency of hemoglobin; those in which the anemia is of the myelophthisic type, and those in which there is an increased degree of blood destruction. Comments on the usefulness of transfusion in secondary anemia in infants are made.

Bass, Denzer and Herman [96] have studied the urobilin excretion in cases of anemia in infants and children. Using the method of Wilbur and Addis, they found the urobilin excretion in stools and urine not to exceed 800 dilution units in normal children between the ages of 1 and 6 years, and not to exceed 1,400 dilution units in normal children from 6 to 11 years of age. In a study of twenty-one cases of anemia in children, they found excessive blood destruction only in a case of hemolytic

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87. Herrman, C.: Idiopathic Aplastic Anaemia, Am. J. Dis. Child. **23**:484 (June) 1922.

88. Spak, H.: Anemia Aplastic, Acta Pediat. **1**:310 (Dec.) 1921.

89. Hummel, H.: Konchennark und Blutfeld in ihrer Beziehung zur Aplastischen Anaemie, Ztschr. f. Kinderh. **32**:285 (May) 1922.

90. Huck, J. G.: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **34**:335 (Oct.) 1923.

91. Sydenstricker, V. P.: Elliptic Human Erythrocytes, J. A. M. A. **81**:113 (July 14) 1923.

92. Sydenstricker, V. P.; Mulherin, W. A., and Houseal, R. W.: Sickle Cell Anaemia: Report of Two Cases in Children, with Necropsy in One Case, Am. J. Dis. Child. **26**:132 (Aug.) 1923.

93. Hatz, A.: Pernicious Anemia in Children, Jahrb. f. Kinderh. **105**:161, 1924.

94. Wischer, D.: Schweiz. med. Wchnschr., 1923, p. 1104.

95. Lucas, W. P., and Hoobler, H. R.: Study of Acute Secondary Anaemias in Infancy, Am. J. Dis. Child. **26**:291 (Oct.) 1923.

96. Bass, M. H.; Denzer, B. S., and Herman, H.: Urobilin Excretion in the Anemias of Infants and Children, Am. J. Dis. Child. **27**:433 (May) 1924.

jaundice. They conclude that blood destruction is not an important feature of anemias of the chlorotic and alimentary types.

The literature, as usual, contains numerous reports of cases of nutritional anemia in infants, due to lack of sufficient iron in the diet. Some of these are mentioned in the appended bibliography.[97] Most of these reports add nothing to our knowledge, but serve to emphasize the comparative ineffectiveness of inorganic iron as a therapeutic measure. More and more, transfusion is being used in the treatment of severe anemia in infants and children with apparently good results.

Not a little discussion has appeared concerning the anemia which develops in infants fed on goat's milk. Blühdorn [98] takes the stand that goat's milk contains no specific influence which causes the anemia, whereas De Rudder [99] believes that goat's milk contains a definite hemolytic agent. Brouwer [100] also holds that the anemia seen in infants fed on a milk diet is due not only to the paucity of iron in milk, but also to a substance that hinders normal blood formation. His observations lead him to believe that goat's milk differs in this respect only quantitatively from cow's milk.

Very interesting in connection with nutritional anemia is the work of Hill,[101] who has studied the relation of pigment and iron in the infant's diet in relation to hemoglobin formation.

Observations made on a series of cases of von Jaksch's anemia are reported by Evans and Happ,[102] by Ramsay [103] and by others.[104]

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97. Lyon, G. M.: Two Cases of So-Called Milk Anemia of Infancy, W. Virginia M. J. **19**:179 (April) 1924; Mackay, H. M. M.: Secondary Anemia in Infancy, Lancet **2**:165 (July 28) 1923; De Angelis, F.: Pediatria **31**:641, 1923; Acuna: Arch. Latino-Am. de Pediat. **17**:1, 1923; Kirsch, O., and Kirsh-Hoffer, E.: Goat Milk Anemia, Wein. klin. Wchnschr. **37**:568 (June 5) 1924.

98. Blühdorn, K.: Zur Frage der Ziegenmilch-Anaemie des Saugling, München. med. Wchnschr. **69**:1220 (Aug. 18) 1922.

99. De Rudder, B.: Goats Milk Anemia, Klin. Wchnschr. **3**:876 (May 13) 1924.

100. Brouwer, E.: Goats Milk in Infant Feeding, Jahrb. f. Kinderh. **103**:51 (Sept.) 1923.

101. Hill, L. W.: Pigment and Iron in the Infant's Diet, Boston M. & S. J. **191**:342 (Aug. 21) 1924.

102. Evans, F. A., and Happ, W. M.: Secondary Anemia in Infants, Bull. Johns Hopkins Hosp. **33**:1 (Jan.) 1922.

103. Ramsay, G. W. St. C.: Anemia with Enlarged Spleen in Infancy and Childhood: Infantile Splenic Anaemia, Brit. J. Child. Dis. **21**:48 (Jan.-March) 1924.

104. Aubon, P.: Pseudoleukemia: Anemia and Hereditary Saturnisms, Arch. de méd. d. enf. **26**:297, 1923. Craig, J., and O'Sullivan, A. C.: Case of Infantile Splenic Anemia, Irish J. M. Sc. **5**:97 (May) 1922. Aubertin, C., and Labbé, R.: Anaemie splenique infantile traite par benzol, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1192, 1922. de Stefano, S.: Contributo allo studio dell' etiopatogenesi dell' anaemie spleniche, infantile, Pediatria **30**:385, 1922. Fanelli, F.: Contributo all'etiopantogenesi del morbo di Cardarelli-Jaksch, Folia med. **16**:601, 1923. Marquard, E.: Ueber Anaemie Pseudo-leukemica Infantum, Arch. f. Kinderh. **72**:251 (May) 1923. Mensi, E.: Essenza e natura della anaemia pseudo-leucemica infantile, Pediatria **30**:652, 1922.

Nothing that is new is contributed by these writers. The general trend of opinion seems to be that von Jaksch's anemia is probably not a disease entity, but a syndrome most often seen in cases of rickets in which there is also present the element of infection. The syndrome may be acute or chronic.

POLYCYTHEMIA

Harbitz [105] presents two cases of myeloerythroblastosis with necropsy reports. The cases referred to were new-born infants who showed ascites and numerous islands of incompletely developed blood corpuscles. A similar condition is reported in a woman, aged 51. Cases of marked functional polycythemia due to congenital heart disease are reported by Stransky [106] and others. Stransky's case differs from the majority of such cases, in that numerous nucleated red cells were observed in the peripheral blood. The condition of this patient, an infant, aged 12 months, is also to be distinguished from the rare condition known as fetal erythroblastosis which shows a polycythemia and many nucleated red cells but which occurs only in the new-born.

No case of true Osler-Vaquez disease in infants or children is mentioned in recent reports, the youngest patient being a boy, aged 12, presented in an article by Minot and Buckman.[107]

Conflicting reports as to the efficacy of irradiation therapy in true erythremia are found in the recent literature. Yet some benefit seems generally to follow exposure to short wave length irradiation, as indicated by the work of Mosenthal,[108] Rydgaard,[109] Schütze,[110] Stolkind [111] and others.

CHLOROMA, MYELOGENOUS LEUKEMIA AND SECONDARY LEUKOCYTOSIS

Cases of myelogenous chloroma are reported by Rowe and Hirschboeck,[112] Foot and Jones [113] and Nasso.[114]. In a series of thirty-seven

105. Harbitz, F.: Hyperplastic Disease of Blood Producing Apparatus, Norsk. Mag. f. Lægevidensk. **84**:211 (March) 1923.

106. Stransky, E.: Clinical Hematology of Infants, Ztschr. f. Kinderh. **35**:195 (April) 1923.

107. Minot, G. R., and Buckman, T. E.: Erythremia (Polycythemia Rubra Vera); Development of Anemia; Relation to Leukemia; Consideration of Basal Metabolism, Blood Formation and Destruction and Fragility of Red Cells, Am. J. M. Sc. **166**:469 (Oct.) 1923.

108. Mosenthal, A.: Roentgen Treatment of Polycythemia, Med. Klin. **19**:1158 (Aug. 19) 1923.

109. Rydgaard, F.: Roentgen Treatment of Primary Polyglobulia, Acta. Rad. **2**:243, 1923.

110. Schütze, J.: Roentgen Treatment of Primary Polyglobulia, Med. Klin. **19**:458 (April 8) 1923.

111. Stolkind, E.: Two Cases of Erythremia Treated by Roentgen Ray, Lancet **1**:1312 (June 30) 1923.

112. Rowe, O. W., and Hirschboeck, F. J.: A Case of Myeloid Chloroma, Am. J. Dis. Child. **24**:239 (Sept.) 1922.

113. Foot, N. C., and Jones, G.: Myelogenous Chloroma, Am. J. Dis. Child. **25**:379 (May) 1923.

114. Nasso, I.: Chloroma in Infant, Pediatria **31**:489 (May 1) 1923.

cases of severe anemia in children reported by Morse,[115] there was only one case of myelogenous leukemia, a fact which serves to illustrate the extreme rarity of this disease in early life.

The pathogenesis of eosinophilia is discussed by Cherkes [116] and De Simone,[117] and observations on the clinical significance of this finding are reported by Hinkelman [118] and by Klienberger.[119]. Holler [120] reports studies of experiments with monocytes, and his findings support the conception that these cells are produced by the reticulo-endothelial apparatus. De La Vega [121] reports observations on the significance of lymphocytosis in infantile vagotonia. He reports fifteen cases in which there occurred marked monocytosis and lymphocytosis with neutropenia.

DISTURBANCES OF THE COAGULATION MECHANISM. HEMORRHAGIC DISEASE OF THE NEW-BORN

Very little that is new concerning hemorrhagic disease of the new-born has developed in the last two years. Cases of this disease are reported by Cruikshank,[122] Rodda,[123] Vignes,[124] Groves,[125] Wing [126] and others. Generally speaking, the intramuscular injection of whole blood, introduced many years ago by Schloss and Commisky, seems to be entirely satisfactory in controlling the bleeding but transfusion may be necessary if there has been much blood loss.

There seems to be a growing tendency to rely on prolongation of coagulation and bleeding time as diagnostic criteria of hemorrhagic disease of the new-born, and on this basis intracranial hemorrhage might

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115. Morse, J. L.: Leukemia and Severe Anemia in Childhood, Boston M. & S. J. **186**:657 (May 18) 1922.
116. Cherkes, D.: Relation Between Blood Eosiniphilia and Vegetative Nervous System, Med. Affairs Harkov. **3**:74, 1923.
117. De Simone, D.: Etio-patogenesi della eosinfilia, Gaz. Int. Med. Chir. **19**:218, 1923.
118. Hinkelman, A. J.: Clinical Significance of Eosiniphilic Cells of Blood, New York M. J. **117**:465 (April 18) 1923.
119. Klienberger, C.: Ueber Eosiniphilie, Deutch. Arch. f. klin. Med. **142**:110 (March) 1923.
120. Holler, G.: Studiem ueber die Stellung der Monozyten, Syst. Bluz. **29**:84, 1923.
121. De La Vega: Estudio del Sistema nervioso vegitativo infantil por medio del examen hematologico, Arch. de card. y Hemat **3**:157, 1922.
122. Cruikshank, J. M.: Hemorrhages of New-Born, Lancet **1**:836, 1923.
123. Rodda, F. C.: Hemorrhagic Disease of New-Born, J. Iowa M. Soc. **13**:511 (Dec.) 1923.
124. Vignes, H.: Gastro-Intestinal Hemorrhages of New-Born, Médecine **4**:538 (April) 1923.
125. Groves, W. R.: Hemorrhage in Newly Born, M. J. Australia **2**:762 (Dec. 30) 1922.
126. Wing, L. A.: Hemorrhages of New-Born, Am. J. Obst. & Gynec. **6**:85 (July) 1923.

frequently be ascribed to this disease as a cause.[127] It must be remembered, however, that the coagulation time and bleeding time may be slightly prolonged without appearance of symptoms. Thus Warwick[128] found the coagulation time and bleeding time to be prolonged in thirteen of 250 new-born infants on the third, fifth and ninth days of life, of whom only two showed symptoms of hemorrhagic disease. Moreover, Greuter[129] found a prolonged coagulation time in 75 per cent. of fifty-three infants showing icterus neonatorum. One of these developed hemorrhagic tendencies.

HEMOPHILIA

Hemophilia in a woman, aged 47, with a very interesting family history and all the classical symptoms of the disease is reported by Warde.[130] The case of a female infant reported by Auricchio[131] is not indisputably hemophilia. The coagulation time was over one and one-half hours, but a definite family history of the disease was wanting and both parents gave a positive Wassermann test. Barney[132] reports seven cases of hematuria, one of perirenal hematoma and one of "retroperitoneal hemorrhage," out of a total of forty-two cases of hemophilia studied at the Massachusetts General Hospital. Perirenal hematoma is usually fatal and is not necessarily accompanied by hematuria.

Rosenbloom[133] points out the danger in the use of arsphenamin in the treatment of syphilis in a patient suffering from hemophilia. Other cases of hemophilia are reported by Fiessinger and Barbillion,[134] Neumann,[135] Vesely,[136] Hynek[137] and others. Though numerous remedial

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127. Ehrenfest, H.: Causation of Intracranial Hemorrhages of New-Born, Am. J. Dis. Child. **26**:503, 1923. Munro, D., and Eustis, R. S.: The Diagnosis and Treatment in Intracranial Hemorrhage in the New-Born, Am. J. Dis. Child. **24**:273 (Oct.) 1922. Losee, J. R.: Hemorrhages in the New-Born, Bull. Lying In-Hosp., New York **12**:100 (July) 1922.

128. Warwick, M.: Value of Routine Determination of Bleeding and Coagulation Time on New-Born Infants, Minnesota Med. **5**:713 (Dec.) 1922.

129. Greuter, W.: Die Blut-gerinnungs-zeit bei Icterus Neonotoriem, Ztschr. f. Kinderh. **35**:210 (June) 1923.

130. Warde, M.: Hemophilia in the Female, Brit. M. J. **2**:599 (Oct. 6) 1923.

131. Auricchio, L.: Hemophilia in Breast-Fed Female Infants, Pediatria **31**:532 (May 15) 1923.

132. Barney, J. D.: The Urological Aspects of Hemophilia, Boston M. & S. J. **189**:486 (Oct. 11) 1923.

133. Rosenbloom, J.: Warning Against the Use of Arsphenamin in the Treatment of Syphilis in a Hemophilic, J. Lab. & Clin. Med. **9**:57 (Oct.) 1923.

134. Fiessenger, N., and Barbillion: Cure of Hemophilia, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:354 (Feb. 24) 1922.

135. Neumann, H.: Hemophilia and Pituitary Extracts, Med. Klin. **19**:115 (Jan. 28) 1923.

136. Vesely, B.: A Case of Hemophilia Inherited in the Male Line, Cas. lek. cesk. **62**:1228 (Nov. 17) 1923.

137. Hynek, K.: Test for Hemophilia and Effective Treatment, Ann. de méd. **14**:122 (Aug.) 1923.

agents, including serum, pituitary gland extract, corpus luteum extract, irradiation, platelet extracts, organ extracts, sodium citrate, etc., have been suggested, no important, certain advance in the treatment of the disease has been reported.

PURPURA

There is a tendency in recent literature to designate those types of purpura associated with a diminished number of blood platelets as thrombocytopenic or thrombopenic purpura. In idiopathic purpura hemorrhagica, the cause of the thrombopenia is unknown and so the name for this disease becomes primary thrombopenic purpura. On the other hand, the purpura that occurs in lymphatic leukemia is also due to a thrombopenia. But here, the thrombopenia in turn is due to a replacement of the platelet forming centers of the marrow by lymphoid tissue, and is thus secondary to some other well recognized condition. Therefore, the purpura seen in lymphatic leukemia becomes secondary thrombopenic purpura.

But purpura identical in clinical manifestations with thrombopenic purpura may occur without reduction of the blood platelets, nonthrombopenic purpura. This also may be primary; idiopathic purpura, purpura simplex; or secondary, symptomatic purpura, rheumatic purpura, septicemic purpura and possibly Henoch's purpura and the purpura accompanying jaundice or such as may occur in scurvy. Practically, the two forms of purpura, thrombopenic and nonthrombopenic, are distinguishable by the bleeding time test. If the purpura is due to a paucity of platelets, then the bleeding time will be prolonged. On the other hand, excepting the new-born and patients showing jaundice or showing manifestations of anaphylaxis, the bleeding time is very rarely prolonged if there is no paucity of platelets.

The value of transfusion, especially the transfusion of unaltered blood, in the treatment of thrombopenic purpura is discussed by Larrabee [138] and by Meulengracht.[139] If the object of the transfusion is to introduce red cells into the circulation, citrated blood may answer the purpose, but if transfusion is given for the purpose of controlling the bleeding by introducing blood platelets, then unaltered blood is preferable. In spite of the fact that one must introduce literally an enormous quantity of blood for the sake of a very small number of platelets, transfusion remains the most effective way of controlling severe bleeding in thrombopenic purpura.

By far the most promising advance in the treatment of primary thrombopenic purpura is the introduction of splenectomy, first advocated

138. Larrabee, R. C.: Transfusion in Purpura Hemorrhagica, J. A. M. A. **80**:838 (March 24) 1923.

139. Meulengracht, E.: Acute Thrombopenic Purpura Treated by Blood Transfusion, Ugesk. f. Læger. **85**:453 (June 28) 1923.

by Kaznelson [140] and recently introduced into America by Brill and Rosenthal.[141] Owing to the fact that primary purpura hemorrhagica may exhibit spontaneous remissions and may even disappear, it is too early, as yet, finally to judge the value of splenectomy as a therapeutic procedure in this disease. Nevertheless reports of clinical improvement and increase of platelets to normal numbers, at least during the period of observation, are encouraging. Patients in whom splenectomy was performed for the relief of this condition are reported by Hitzrot,[142] Bass and Cohen,[143] Bowen,[144] Brill,[145] Vogel [146] and others. In the two cases reported by Brill, the blood showed thrombopenia again at the end of two weeks after operation but no clinical symptoms had returned at the end of eight months. In three of Vogel's cases there was continued symptomatic relief, though the increase of platelets was only temporary. In a fourth case splenectomy was entirely ineffective: the patient died from hemorrhage after the operation. The consensus of opinion at present seems to be that splenectomy should be preceded, and if necessary followed by transfusion in order to minimize operative hazards.

An excellent clinical review of ten cases of various types of primary purpura is given by Poynton, Thursfield and Paterson.[147] Fulminating purpura in early life is reported by König,[148] McConnell and Weaver,[149] Portu [150] and others. Schoenberger,[151] Stansfield,[152] and Dwyer [153]

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140. Kaznelson, P.: Indication for Splenectomy in Purpura Hemorrhagica, Wien. Arch. f. inn. Med. **7**:87, 1923.

141. Brill, N. E., and Rosenthal, N.: Curative Treatment by Splenectomy of Chronic Thrombocytopenic Purpura Hemorrhagica, Am. J. M. Sc. **166**:503 (Oct.) 1923.

142. Hitzrot, J. M.: Splenectomy in Hemorrhagic Purpura; Idiopathic Purpura Essential Thrombopenic (Frank); Purpura Hemorrhagic protopathique (Hayem), Ann. Surg. **78**:185 (Aug.) 1923.

143. Bass, M. H., and Cohen, P.: Thrombocytopenic Purpura Hemorrhagica Successfully Treated by Splenectomy, Am. J. Dis. Child. **27**:332 (April) 1924.

144. Bowen, B. D.: A Case of Chronic Purpura Hemorrhagica with Therapeutic Splenectomy, Bull. Buffalo Gen. Hosp. **1**:1, 1923.

145. Brill, N. E.: Footnote 141.

146. Vogel, R.: Splenectomy in Blood Diseases, Deutsch. Ztschr. f. Chir. **180**:37, 1923.

147. Poynton, F. J.; Thursfield, H., and Paterson, D.: The Severe Blood Diseases of Childhood: Purpura, Brit. J. Dis. Child. **19**:57 (April-June) 1922.

148. König: Fulminating Purpura in an Infant, Ztschr. f. Kinderh. **32**:282 (May) 1922.

149. McConnell, G., and Weaver, H. L.: Purpura Fulminans During Convalescence from Scarlet Fever, J. A. M. A. **78**:165 (Jan. 21) 1922.

150. Portu, P. E.: Purpura with Ventricular Hemorrhage, Arch. latino-am. de pediat. **16**:562, 1922.

151. Schoenberger, M.: Thrombopenic Purpura in Children, Arch. f. Kinderh. **73**:157, 1923.

152. Stansfield, O. H.: Case of Secondary Purpura Hemorrhagica with Remarkable Blood Changes, Boston M. & S. J. **187**:739, 1923.

153. Dwyer, H. L.: Purpura Fulminans, J. A. M. A. **78**:1187 (April 22) 1922.

report cases of purpura with unusual blood and clinical findings. Cases of Henoch's purpura are reported by Kilgour,[154] Wilson [155] and Millard.[156]

Gram [157] reports a case of primary nonthrombopenic purpura (Werlhoff's disease) apparently cured by repeated protein shock. Again and again, intimations occur in the literature that such diseases as Henoch's purpura and morbus maculosus Werlhofii are manifestations of allergy in a previously sensitized person, and that they might be cured by some process of desensitization. Nevertheless, no one as yet has been able consistently to secure improvement by such means, and the etiology of these conditions remains almost as obscure and the treatment almost as unsatisfactory as when they were first described.

TRANSFUSION IN THE TREATMENT OF ANEMIA

No attempt is made here to review the voluminous literature of the subject of transfusion. Only those phases especially concerned with infants and children can be considered. Kerr's [158] article on the history of transfusion, however, should be read by any one interested in the story of the development of the technic of transfusion.

To the pediatrician, by far the most important contribution made in recent years in this field is the work of Sansby and Siperstein.[159] These investigators showed first by experiments on rabbits that the red corpuscles of citrated blood introduced into the peritoneal cavity are absorbed practically quantitatively into the general circulation and that this procedure can be carried out without harm. Siperstein [160] then reported the favorable results he obtained by intraperitoneal transfusions given to infants. Since then, Siperstein and Sansby,[161] Meyer,[162] Opitz,[163] Ruh [164] and others have shown the value of the procedure in

154. Kilgour, D.: Henoch's Purpura, Canad. M. A. J. **14**:302 (April) 1924.
155. Wilson, S.: Henoch's Purpura, J. Mich. M. S. **21**:136 (March) 1921.
156. Millard, R. J.: Henoch's Purpura, M. J. Australia **2**:446 (Oct. 14) 1922.
157. Gram, H. C.: Ein nach wiederholten Proteinschock geheilter Fall von Werlhofscher Krankheit, Ztschr. f. klin. Med. **95**:51 (Sept.) 1922.
158. Kerr, W. M.: History of Blood Transfusion, U. S. Naval M. Bull. **16**:465 (March) 1922.
159. Sansby, J. M., and Siperstein, D. M.: Intraperitoneal Transfusion with Citrated Blood, J. A. M. A. **80**:1763 (June 16) 1923.
160. Siperstein, D. M.: Intraperitoneal Transfusion with Citrated Blood, Am. J. Dis. Child. **25**:202 (March) 1923.
161. Siperstein, D. M., and Sansby, J. M.: Intraperitoneal Transfusion with Citrated Blood, Am. J. Dis. Child. **25**:107 (Feb.) 1923.
162. Meyer, L. F.: Intraperitoneal Transfusion of Blood, Jahrb. f. Kinderh. **105**:188, 1924.
163. Opitz, H.: Intraperitoneal Injection of Blood, Klin. Wchnschr. **3**:784 (April 29) 1924.
164. Ruh, H. O., and McClelland, J. E.: Intraperitoneal Transfusion in Infants, Ohio State M. J. **19**:780 (Nov.) 1923.

the treatment of anemia in infants. Red corpuscles introduced into the peritoneum are absorbed to a large extent through those lymphatic vessels which establish drainage between the peritoneum and the cisterna chyli (Ruh).

Although there is not the slightest evidence even to suggest that corpuscles introduced into the peritoneum become "naturalized," so that compatibility tests may be dispensed with, one finds reports suggesting that there is no need of grouping the blood which is given into the peritoneal cavity. Thus Meyer [162] reports twenty-five cases in which blood was given to young children by the peritoneal method: no compatibility tests were made and no ill effects resulted. The idea that blood grouping may be done away with in using intraperitoneal transfusions in early life is kin to the general conception that tests for compatibility are unnecessary in infancy anyhow, especially if blood from a parent be used. The truth of the matter is that hemolytic reactions are rare in early life, and they are rare for the following reason: the serum agglutinins and hemolysins in early life are present usually in low concentration and consequently are generally incapable of causing hemolysis of the infused cells whatever their group. This rule is not infallible, however, and a severe or even fatal hemolytic reaction may occur if cells of an inconsistent group are introduced. That such an occurrence is extraordinary should not constitute a rationale for dispensing with compatibility tests.

Moreover, it does not follow that because blood from a given donor has once been given with impunity, the same donor may safely be used again, for the same patient. Robertson and Rous [165] have shown that in rabbits antibodies may develop following repeated transfusions from the same donor and may actually cause hemolytic reactions. Such reactions have been described in man; for example, the two cases reported by Astrowe,[166] one an infant, in which severe hemolytic reactions followed the second transfusions from donors whose blood corpuscles had proved compatible by direct test in each case prior to the first transfusions. Before red corpuscle are introduced into the circulation it must be shown every time in every case, regardless of age, that the cells of the donor will not be hemolyzed by the serum of the recipient.

Though transfusion of blood by the peritoneal route will permit the use of transfusion where its use might otherwise be extremely difficult or out of the question, still another possible route for the introduction

165. Robertson, O. H., and Rous, P.: Sources of the Antibodies Developing After Repeated Transfusion, J. Exper. Med. **35**:141 (Feb.) 1922.

166. Astrowe, P. S.: Hemolysis Following Transfusion, J. A. M. A. **79**:1511 (Oct. 28) 1922.

of blood has been recently described. Sidbury [167] used the umbilical vein for introducing blood into an infant, aged 4 days, suffering from hemorrhagic disease of the new-born. Uneventful recovery followed.

Until recently, transfusion has not been extensively used in infants and children except for the purpose of controlling bleeding or for the relief of very severe anemia. But the beneficial effects of blood are apparently not confined to supplying thromboplastic substances and oxygen carriers. Leebron [168] reports excellent results following the use of transfusion in malnutrition and infantile atrophy, and more recently Marriott [169] and Hess [170] have advocated its use in the treatment of infants suffering from acute dehydration and toxemia. Though, on empirical grounds, transfusion in such cases is certainly beneficial, the rational basis for its use is not apparent unless it be, perhaps, that some of the symptoms are due to a diminished blood volume. If such is the case, the situation might well be more effectively relieved by introducing blood rather than salt solution or glucose.

Concerning the amount of blood to be introduced into infants and children, important information is given by the report of Halbertsma.[171] According to this investigator, 15 c.c. of blood per kilogram of body weight will cause a rise of the red cell count of about one million in infants and young children. Hence the generally accepted maximum dosage for infants, 15 c.c. of blood per pound of body weight, should permit an increase of somewhat over two millions of red cells per cubic millimeter of blood.

BLOOD PARASITES

Malaria is the only disease due to a special blood parasite described in the recent literature. A case of congenital malaria due to quartan parasites is reported from Colorado by Forbes.[172] Other papers dealing with malaria in infants and young children are those by Mulherin and Mulherin,[173] by Chimisso [174] and by Dentici.[175]

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167. Sidbury, J. D.: Transfusion Through the Umbilical Vein in Hemorrhage of the New-Born, South. M. J. **16**:676 (Sept.) 1923.
168. Leebron, J. D.: Blood Transfusion in Malnutrition and Infantile Atrophy, New York M. J. **117**:298 (March 7) 1923.
169. Marriott, W. McK.: Food Requirements of Malnourished Infants, J. A. M. A. **83**:600 (Aug. 23) 1924.
170. Hess, J. H.: Discussion, J. A. M. A. **83**:602 (Aug. 23) 1924.
171. Halbertsma, T.: The Amount of Blood to be Transfused in Anemia of Children, Am. J. Dis. Child. **24**:269 (Oct.) 1922.
172. Forbes, R. P.: Congenital Malaria, Am. J. Dis. Child. **25**:150 (Feb.) 1923.
173. Mulherin, W. A., and Mulherin, F. X.: A Few Observations on Malaria in Infancy, J. A. M. A. **78**:1873 (June 17) 1922.
174. Chimisso, L.: Chronic Malaria in Children, Riforma med. **38**:241 (March 13) 1922.
175. Dentici, S.: Radio Stimulation of Spleen in Chronic Malaria, Tumori **9**:19 (July) 1922.

DISEASES OF THE SPLEEN AND LYMPH NODES (EXCEPT TUBERCULOSIS).

ACUTE INFECTIOUS MONONUCLECSIS (GLANDULAR FEVER)

Longcope [176] reports ten cases of acute infectious mononucleosis. Three cases of the same disease closely simulating acute lymphatic leukemia are reported by Cross.[177] This disease, at onset, may be confused with acute lymphatic leukemia in that both may show generalized lymph node enlargement, splenomegaly and leukocytosis with a preponderance of lymphocytes. Glandular fever terminates favorably, however. Moreover, in glandular fever, the number of blood platelets is not diminished, and there may be polycythemia, findings inconsistent with acute lymphatic leukemia.

LYMPHATIC LEUKEMIA

Minot and Isaacs [178] report an extensive statistical analysis of 155 cases of lymphatic leukemia; ninety-eight chronic, fifty-seven acute. Their study illustrates the relative preponderance of the acute form in early life and of the chronic form in later life. Smaller series of cases, but cases especially in infants and children are reported by Poynton, Thursfield and Paterson,[179] Bazan and Vallino,[180] Condat,[181] Cohan [182] and others.

Nothing new pertaining to the clinical features of the disease or to the etiology has been reported. Although one occasionally reads of attempts to treat acute lymphatic leukemia by irradiation, as yet no success has been reported and the treatment of this condition remains entirely unsuccessful.

The recent literature contains no account of Hodgkin's disease or sarcoma of the spleen in early life, but cases of Gaucher's disease are reported by Lippman [183] and by Monteleone.[184]

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176. Longcope, W. T.: Infectious Mononucleosis, Am. J. M. Sc. **164**:781 (Dec.) 1922.

177. Cross, J. G.: Conditions Stimulating an Acute Leukemia, Minnesota Med. **5**:579 (Oct.) 1922.

178. Minot, G. R., and Isaacs, R.: Lymphatic Leukemia; Age Incidence; Duration and Benefits Derived from Irradiation, Boston M. & S. J. **191**:1 (July 3) 1924.

179. Poynton, F. J.; Thursfield, H., and Paterson, D.: The Severe Blood Diseases of Children—Leukemia, Brit. J. Child. Dis. **19**:128, 1923.

180. Bazan, F., and Vallino, M. T.: Consideraciones sobres un caso de leucemia linfatica subaguda, Semana méd. **2**:92 (July 13) 1922.

181. Condat: Acute Leukemia in Children, Arch. de méd. d'enf. **26**:286 (May) 1923.

182. Cohan, W.: Subacute Lymphatic Leukemia in a Boy of Three, Semana méd. **2**:580 (Sept. 20) 1923.

183. Lippman, H.: Zur Klinischen Diognose des "Morbus Gaucher," Med. Klin. **18**:1607 (Dec. 17) 1922.

184. Monteleone, E.: Sul marto de Gaucher, Policlinico **29**:164, 1922.

HEMOLYTIC JAUNDICE

Excellent monographs on this disease have been written in recent years by Tileston [185] and by Meulengracht.[186] Cowen [187] reports a family of nineteen persons who showed varying degrees of jaundice, splenomegaly and anemia. Every one of the nineteen showed increased fragility of the red corpuscles to hypotonic sodium chlorid solutions. Splenectomy had been performed on thirteen of these patients with marked benefit.

Although splenectomy seems to be accepted as the best treatment for cases of hemolytic jaundice with well marked symptoms, Comby [188] suggests the use of irradiation therapy, and Littlejohn [189] reports improvement following this form of treatment.

Semeran [190] reports the interesting finding of a hypocholesterinemia in cases of hemolytic jaundice. The cholesterin content of the blood increases somewhat after splenectomy.

SPLENIC ANEMIA

Though Banti's disease was originally described as a primary endophlebitis of the splenic veins resulting in cirrhosis of the spleen, belief is gaining ground that obstruction anywhere in the portal system results ultimately in cirrhosis of both the spleen and the liver and the subsequent development of two characteristic features: (1) symptoms of mechanical obstruction, such as ascites and venous engorgement, and (2) anemia with a low color index and leukopenia. Thus cirrhosis of the liver, Banti's disease, cirrhosis of the spleen and other diseases with similar pathology might all ultimately exhibit the same syndrome, so-called splenic anemia.

Chaney [191] found in the study of spleens removed from sixty-nine patients with splenic anemia at the Mayo Clinic that the principal pathologic change was a generalized fibrosis with diminution in the number and size of the malpighian bodies. Sizuka [192] found that the same atrophy of the malpighian bodies could be produced by injections of atropin.

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185. Tileston, W.: Hemolytic Jaundice, Medicine **1**:355 (Aug.) 1922.
186. Meulengracht, E.: Der chronische heriditaire haemolytische Ikterus, Monograph, Leipsic, 1922.
187. Cowen, S. O.: Familial Hemolytic Splenomegaly, M. J. Australia **9**:545 (Nov. 11) 1922.
188. Comby, J.: Hemolytic Jaundice in Children, Arch. de méd. d. enf. **25**:99 (Feb.) 1922.
189. Littlejohn, E. S.: Familial Hemolytic Splenomegaly Treated by X-Rays, M. J. Australia **1**:669 (June 23) 1923.
190. Semeran, M.: Study of Disturbances of Hemopoietic System, Gaz. lek. **35**:686, 1923.
191. Chaney, W. C.: Splenic Anaemia, Am. J. M. Sc. **165**:856 (June) 1923.
192. Sizuka, N.: Banti's Disease, Japan M. World **8**:239, 1922.

Reviews of the symptomatology, pathology and treatment of Banti's disease are given by Comby [193] and by Rodrigo.[194] According to De Meuron [195] true Banti's disease is rare in children. He reports one case with necropsy findings and states that he has been able to find in the literature only forty cases of this disease, corresponding exactly with Banti's original description.

De Stefano [196] reports thirteen cases of splenic anemia due to syphilis, and six others in which both syphilis and tuberculosis were etiologic factors, and Weber [197] describes cases in which the liver was mainly affected with secondary enlargement of spleen and anemia.

SPLENECTOMY

The indications for and effects of splenectomy are reviewed at length by Krumbhaar,[198] Bartlett,[199] Vogel,[200] Bowen,[201] Brill,[202] Carslaw [203] and others. Of 1,073 cases of various diseases presented by Krumbhaar in which splenectomy had been done, 177 apparently had been cured and 591 improved by the procedure. According to Krumbhaar, splenectomy is most valuable in hemolytic jaundice in which disease it removes the chief agent of blood destruction. Bartlett points out that splenectomy is more often indicated in early life than is usually supposed. From his series of fifty-one children in whom splenectomy had been done, he concludes that hemolytic jaundice is the condition which is most constantly relieved by this procedure but that Gaucher's disease and splenic anemia also may be cured by splenectomy. Vogel [200] and Carslaw [203] reach the same conclusions. Vogel, Brill and Bowen and Denzer report improvement following splenectomy in cases of idiopathic thrombopenic purpura, and Vogel reports improvement in a case of lymphatic leukemia following splenectomy.

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193. Comby, J.: Present Status of Banti's Disease in Children, Arch. de méd. d'enf. **26**:39 (Jan.) 1923.

194. Rodrigo, D.: Banti's Disease in Children, Arch. españ. de pediat. **7**:321 (June) 1923.

195. De Meuron, M.: Banti's Disease in a Boy Aged Ten, Arch. de méd. d'enf. **26**:416, 1923.

196. De Stefano, S.: Pediatria **30**:385, 1922.

197. Weber, F. P.: Banti's Disease, Brit. J. Dis. Child. **20**:78, 1920.

198. Krumbhaar, E. B.: Hemolytopoietic System in Primary Anemia with Further Note on Value of Splenectomy, Am. J. M. Sc. **166**:329 (Sept.) 1923.

199. Bartlett, F. H.: Indications for the Removal of the Spleen in Infants and Children, Am. J. Dis. Child. **23**:283 (April) 1922.

200. Vogel, R.: Splenectomy in Blood Diseases, Deutsch. Ztschr. f. Chir. **180**:37, 1923.

201. Bowen, B. D.: Footnote 144.

202. Brill, N. E.: Footnote 141.

203. Carslaw, J.: Surgical Treatment of Nontraumatic Affection of the Spleen, Brit. M. J. **2**:1204 (Dec. 23) 1922.

The consensus of opinion seems to be that splenectomy in children is indicated under the following conditions: in hemolytic jaundice when the disease is sufficiently severe to cause symptoms, in Gaucher's disease, in splenic anemia, especially when this is of Banti's type, and in suitable cases of idiopathic thrombopenic purpura. On the other hand, in spite of the fact that the enlargement of the spleen may be considerable and that improvement has been reported to follow its removal, splenectomy is generally held to be of doubtful value or to be contraindicated in the leukemias and in polycythemia, in acute infections, in Hodgkin's disease and in von Jaksch's anemia.

CORRECTION

The case numbers, in the article by Dr. Richard M. Smith, "Roentgen-Ray Examinations in Diseases of the Kidney," in the December issue, are incorrect. The figures and case numbers should appear as follows:

Fig. 1 (Case 4); Fig. 2 (Case 5); Fig. 3 (Case 6); Fig. 4 (Case 7); Fig. 5 (Case 8); Fig. 6 (Case 9); Fig. 7 (Case 13); Fig. 8 (Case 12); and Fig. 9 (Case 11).

Abstracts from Current Literature

Anatomy and Physiology

THE NORMAL AND PATHOLOGIC ANATOMY OF THE SELLA TURCICA AS REVEALED BY ROENTGENOGRAMS. JOHN D. CAMP, Am. J. Roentgenol. **12**:143 (Aug.) 1924.

An exact technic is required because of the multiplicity of bone structure about the deep seated sella, which is relatively small. The author centers a small cone along Reid's base line 2.5 cm. in front and 1.88 cm. above the external auditory meatus. To prevent distortion, the sagittal plane of the head must be parallel with the film and perpendicular to the principal ray. The usual types of sella are the circular, flat and oval. The circular is the usual type in children. In children also the posterior clinoid process is inconspicuous, due to incomplete development of the sphenoid bone, and the floor of the pituitary fossa is formed by solid substance of the basisphenoid bone before the formation of the sphenoid sinus takes place, and this does not show signs of erosion as early as does the adult structure.

The size of the normal sella varies greatly so that early pathologic changes are difficult to diagnose. The range of the anteroposterior distance in this series was from 0.5 to 1.6 cm. and that of the depth from 0.4 to 1.2 cm.; this averaged 1.06 for the anteroposterior and 0.81 for the vertical measurement. Normal variations in the shape of the clinoid process are not uncommon, and the bony union between the anterior and posterior clinoid process produces a "bridged sella" in 5.5 per cent. of the cases. Owing to the deformity of the sella, some distinction between intrasellar and extrasellar tumors can be made, but a localization of extrasellar tumors by this differentiation is not possible. Anatomic specimens always reveal more bone destruction than can be recognized by the roentgenogram.

STULIK, Chicago.

INTESTINAL CHEMISTRY. I. THE ESTIMATION OF INTESTINAL REDUCTIONS. OLAF BERGEIM, J. Biol. Chem. **62**:45, 1924.

The author presents a new method of determining the extent or degree of the chemical reduction existent in the gastro-intestinal tract. This is accomplished by giving with the meals a definite proportion of ferric hydroxid (usually 1 per cent.). The ferric hydroxid is practically unabsorbed, but is in part reduced to a ferrous salt. The percentage of the iron which has been reduced is determined colorimetrically by adding potassium thiocyanate to duplicate specimens of an acid extract of stool, one of which has been previously oxidized with potassium permanganate solution. The percentage of ferric hydroxid reduced gives an index of the extent of intestinal putrefaction.

INTESTINAL CHEMISTRY. II. INTESTINAL REDUCTIONS AS MEASURES OF INTESTINAL PUTREFACTION, WITH SOME OBSERVATIONS ON THE INFLUENCE OF DIET. OLAF BERGEIM, J. Biol. Chem. **62**:49, 1924.

This paper deals with experiments on rats, who were fed various diets, containing also 1 per cent. ferric hydroxid. The degree of intestinal reduction (putrefaction) was determined. The reduction was found to take place wholly in the large intestine in a rat fed only meat, and not less than two-

thirds in the large intestine on diets partly or wholly carbohydrate. No reduction occurred in the stomach and very little in the upper part of the small intestine.

When diets were fed containing starch and 20 per cent. of different proteins, varying degrees of reduction occurred: namely, egg albumin 71 per cent., meat 63 per cent., casein 19 per cent., gelatin 40 per cent. The high reduction with egg, may be due to the high sulphur content, with hydrogen sulphid formation.

Of the carbohydrates, lactose and dextrin which remain longer in the intestine than other sugars, led to less reduction, probably by reason of prevalence of fermentation over putrefaction.

Milk, fruits and vegetables tended to lessen the reduction.

Salicylic acid, beta naphthol and kaolin, representing intestinal antiseptics, failed to produce any appreciable change in the reduction.

This method has an advantage over the "indican" index of intestinal putrefaction by reason of its being independent of the tryptophan content in the diet and of its being better expressed quantitatively.

HIGGINS, Cincinnati.

THE INFLUENCE OF THE SUPRARENAL GLAND ON THE THYMUS. II. DIRECT EVIDENCE OF REGENERATION OF THE INVOLUTED THYMUS FOLLOWING DOUBLE SUPRARENALECTOMY IN THE RAT. HENRY L. JAFFE, J. Exper. Med. **40**:619, 1924.

In each of thirteen rats, a portion of the right lobe of the thymus was removed under ether anesthesia, and bilateral suprarenalectomy was done thirteen to seventeen days later. The animals died or were sacrificed seventeen to thirty-nine days after suprarenalectomy. The histologic appearance of the remaining portions of the thirteen thymuses at necropsy was compared with that of the fragments obtained at operation.

The ages of the rats at death varied from 282 to 427 days. The thymus in the normal rat begins to involute between the eightieth and ninetieth days of age.

Histologic examination of the fragments of thymus removed at operation showed that involution of the gland had begun in all thirteen rats, being slight in one, moderate in four, and well advanced in eight. Following bilateral suprarenalectomy, the remaining portions of the thymuses at necropsy showed histologic evidences of secondary hyperplasia and regeneration, the regeneration being moderate in one rat and marked in the other twelve.

To determine whether or not partial thymectomy alone will induce compensatory secondary hyperplasia in an involuting thymus gland, several rats were partially thymectomized and sacrificed two weeks later. Practically no differences were found in the microscopic appearance of the fragments of gland removed at operation and the remaining portions removed at necropsy.

MCCLURE, Evanston, Ill.

Pathology, Bacteriology and Biochemistry

A BACTERIAL DISEASE OF ADULT HOUSE FLIES. R. W. GLASER, Am. J. Hygiene **4**:411 (Sept.) 1924.

The author here describes, for the first time, a bacterial disease of adult house flies, which is sporadic in its appearance and caused by an organism named by the author *Staphylococcus muscae*.

Experimentally, about 50 per cent. adult flies can be infected. Males are more susceptible than females. Those so infected live, on an average, sixteen days.

Reasons are advanced that not much may be expected from the disease from an economic standpoint.

SCOTT, Pittsburgh.

CHANGES IN THE ARTICULAR SURFACES IN TUBERCULOUS AND IN PYOGENIC INFECTIONS OF JOINTS. D. B. PHEMISTER, Am. J. Roentgenol. **12**:1 (July) 1924.

Roentgenography, an important aid in detection of proliferative, absorptive and atrophic changes in the pathology of tuberculous and pyogenic arthritides, has been made so little use of that the roentgenologist has been compelled to go back to work on joint pathology antedating the roentgenogram, for aid in interpretation. The author states that the old idea of the destruction of cartilage beginning at the points of contact and pressure and extending to the free cartilage, holds only in pyogenic infections, while in tuberculous arthritis of joints with both free and contact surfaces, as a rule, the cartilage is first destroyed where it is unapposed and often is best protected and stands longest at the points of contact and greatest pressure. In both conditions the articular cartilage is involved secondarily to the primary infection in the bone or synovial lining.

Lamination of bone is not considered pathognomonic of tuberculous infection, and is not infrequent in other infections especially in localized pyogenic osteomyelitis. In tuberculous arthritis at the points of contact and pressure, the attack of granulations on the cartilage is usually from beneath, resulting in absorption of bony cortex and detachment of the cartilage.

In pyogenic infection the proteolytic ferments present assist in digestion of dead cartilage. In tuberculous arthritis the dead cartilage, which has been detached or which is located on sequestra, may stand for months or years unless erosion takes place because of improper mobilization or because of the action of granulations on the separated cartilage. Secondary invasion of the bone resulting in sequestra bordering on the articular surface is rare in pyogenic arthritis, but common late in tuberculous arthritis. In tuberculosis the points of contact and pressure are apt to have bilateral bone invasion with formation of "kissing sequestra."

In the roentgenogram generally, the evidence of disappearance of cartilage and cortex at the points of contact and pressure first suggest pyogenic arthritis, while evidences of their preservation longest in these regions and of disappearance in unapposed regions are indicative of tuberculous arthritis.

STULIK, Chicago.

ACID-FORMING STREPTOCOCCI AS INDICES OF FOMITES POLLUTION. C. E. A. WINSLOW and DOROTHEA H. SANJIYAN, J. Bacteriol. **19**:513, 1924.

The authors present evidence to show a general relation between the presence of acid-forming streptococci on various classes of objects, and the extent to which these objects have been exposed to recent salivary pollution.

Streptococci were isolated from 62 per cent. of objects exposed to mouth contamination, from 42 per cent. of objects exposed to hand contamination, and from 10 per cent. of objects not recently contaminated.

The examination in a single dilution of three swabs taken from adjacent areas on the surface of the object in question gave results with the least margin of error.

THE EFFECT OF ENVIRONMENTAL CHANGES ON THE GROWTH, MORPHOLOGY, PHYSIOLOGY AND IMMUNOLOGICAL CHARACTERS OF BACTERIUM TYPHOSUM. CHARLES A. STUART, J. Bacteriol. **19**:589, 1924.

Ten strains of *Bacterium typhosum,* isolated from various sources, were examined for the effects of environmental changes on characteristics of this organism.

It was found that the physiologic reactions are the only ones remaining unchanged under conditions affecting all other characteristics of the species. These reactions are then to be relied on more than any other feature in the differentiation of *Bacterium typhosum.*

The following observations were made:

1. Power of growth varies with different strains.
2. Morphology varies with differences in composition of the medium and temperature.
3. Variation in immunologic properties occurs only when the conditions under which the antigens are cultivated are favorable or unfavorable.
4. All strains in all environments are quite constant in physiologic reactions.
5. It is possible to get great variation in any one character of a strain without getting variations in all characters of that strain.

WESTLUND, Chicago.

THE INFLUENCE OF SODIUM CHLORID ON THE LEVEL OF BLOOD URIC ACID. VICTOR JOHN HARDING, KATHLEEN DREW ALLIN and H. B. VAN WYCK, J. Biol. Chem. **62**:61, 1924.

When 15 gm. of sodium chlorid was added to a diet, the uric acid content of the blood decreased. At the same time the serum protein of the blood diminished and the sodium chlorid increased.

ON THE PASSAGE OF BORIC ACID THROUGH THE SKIN BY OSMOSIS. LOUIS KAHLENBERG, J. Biol. Chem. **62**:149, 1924.

When the feet were immersed in a solution of boric acid containing alcohol, boric acid appeared in the urine (0.01 to 0.001 per cent.). There was no absorption when salts of boric acid were used.

FAT-SOLUBLE VITAMINS. XIX. THE INDUCTION OF CALCIFYING PROPERTIES IN A RICKETS-PRODUCING RATION BY RADIANT ENERGY. H. STEENBOCK and M. T. NELSON, J. Biol. Chem. **62**:209, 1924.

White rats, aged 24 to 36 days, were fed on a diet which produced rickets. After twenty-five or fifty days on this diet, the food was irradiated by exposure to a quartz mercury vapor lamp. The animals receiving the irradiated diet for as short a period as six days showed a deposit of calcium in the epiphyses (healing rickets) when the bones were examined histologically.

HIGGINS, Cincinnati.

THE INFLUENCE OF THYROIDECTOMY, GONADECTOMY, SUPRARENALECTOMY, AND SPLENECTOMY ON THE THYMUS GLAND OF RABBITS. DAVID MARINE, O. T. MANLEY and EMIL J. BAUMANN, J. Exper. Med. **40**:429, 1924.

This paper refers to work and views of other writers bearing on these subjects, and reports an analysis of data of 373 protocols of experiments on rabbits. The anatomic condition of the thymus found at necropsy was checked by microscopic examination. In the study the rabbits are divided into four age groups: (1) under 7 months, (2) from 7 to 13 months, (3) from 13 to 19 months and (4) over 19 months, the age taken being that at the time of operation.

Seventy-one of the rabbits were splenectomized as the only operation or in combination with other operations, but since no definite influence on the thymus was found, all splenectomized rabbits are included either under normal, when splenectomy was the only operation, or under the associated gland when combined with other organ removal.

The normal group consisted of 122 rabbits, including 23 with splenectomy. The authors' summary follows:

Thyroidectomy hastens, while gonadectomy delays, but does not permanently prevent, involution of the thymus.

Suprarenalectomy alone not only delays involution of the thymus and lymphoid tissue but may cause their regeneration. Thyroidectomy prevents this reaction even after combined suprarenalectomy and gonadectomy.

Suprarenalectomy plus gonadectomy is a more powerful stimulus for thymus and lymphoid regeneration than either of these influences alone.

The combined effect of these two factors results in certain lymphoid and thymus hyperplasia in rabbits, which persists until regeneration of accessory interrenal tissue corrects the physiologic defect. The syndrome thus experimentally produced resembles status lymphaticus, and is believed to depend mainly on a partial loss of certain functions of the interrenal and sex glands rather than of the chromaffin tissue.

The normal and abnormal lymphoid and thymic hyperplasias of infancy and childhood are believed to be manifestations of a functional underdevelopment of the interrenal and sex glands of varying intensity.

The so-called lymphatic constitution which underlies or accompanies exophthalmic goiter, Addison's disease, and acromegaly also appears to be dependent on a partial suppression of certain functions of the interrenal and sex glands.

STUDIES ON THE BIOLOGY OF STREPTOCOCCUS. IV. THE OCCURRENCE OF STREPTOCOCCUS SCARLATINAE IN CONVALESCENCE AND IN THE COMPLICATIONS OF SCARLET FEVER. FRANKLIN A. STEVENS and A. R. DOCHEZ, J. Exper. Med. **40**:493, 1924.

Bliss and Tunnicliff previously obtained streptococci from the throats of convalescent scarlet fever patients, which agglutinated with scarlatinal immune serums.

The authors employed the agglutination reaction for further study of the distribution of these streptococci in the convalescence and in the complications of scarlet fever patients. The material used included throat cultures from scarlet fever patients, taken between the third and sixth day after onset of the angina, and during convalescence, including in the latter group many previously found positive in the acute group. Serums were prepared from the first five strains isolated and from a strain obtained from Bliss. Of the throat cultures of the forty patients in the acute group 87.5 per cent. showed hemolytic streptococci; 74.3 per cent. of these strains were agglutinated by type immune serums.

Of the thirty-eight patients cultured at the end of the quarantine period, including nineteen who were found positive in the acute stage, 29 per cent. were carriers of hemolytic streptococci which were agglutinated by the serums.

Hemolytic streptococci were found most frequently in the throat in convalescent patients in whom the tonsillar inflammation had not entirely subsided.

From the bacteriologic study of the complications, the authors are of the opinion that these may be due to the original scarlatinal strain or to a secondary infection with pyogenic strains of streptococci.

THE BLOOD PLATELETS IN PNEUMOCOCCUS INFECTIONS. HOBART A. REIMANN, J. Exper. Med. **40**:553, 1924.

Using the method of Thomsen, with certain modifications in technic, the blood platelets were counted during the course of pneumonia in man and also in several rabbits experimentally infected with pneumococci. The average count for normal human blood was found to be 350,000 per cubic millimeter with slight variations in the same person. Observations in thirteen cases of lobar pneumonia and three cases of bronchopneumonia in man, and in two cases where pneumococcus septicemia was produced in rabbits are reported.

In all the uncomplicated cases of lobar pneumonia with recovery, there was a thrombopenia of from 125,000 to 243,000 per cubic millimeter during fever, and a thrombocytosis following the return of the temperature to normal. The

increase in platelets usually began several hours after the crisis and continued during the following six to nine days. The count returned to normal in about the same number of days.

In one mild case of bronchopneumonia, a normal platelet count was found; in another a fluctuation of from 160,000 to 360,000. In a fatal case, counts of 90,000 and 70,000 were obtained.

In a rabbit receiving an overwhelming dose of pneumococci, a diminution in the platelet count was found twenty-four hours after infection with a further rapid decrease until death occurred. In a rabbit receiving a much smaller dose there was a slight diminution in the platelet count, with a postfebrile increase.

The platelets in general are smaller and contain more granules during the thrombopenic stage of pneumonia.

THE RELATION OF DOSE OF BACTERIA TO GROUP INFECTION. ARTHUR L. BLOOMFIELD and AUGUSTUS R. FELTY, J. Exper. Med. **40**:679, 1924.

While "carriers" are to be regarded as storehouses of bacteria which may lead to the production of disease in other people, it is evident that some particular combination of circumstances is necessary before secondary carriers or instances of clinical disease will develop. The exact analysis of the factors which determine such spread of infection is of interest from a biologic standpoint, and of the utmost practical importance in the standardization of public health measures.

In a previous paper, the authors suggested that the dose of bacteria and the degree of their vegetative activity were at least two factors of significance in determining whether or not infection will develop in a susceptible host. The experiments reported in the present paper extend and confirm these conclusions, especially with reference to the relation of dose of bacteria to group infection.

Hemolytic streptococci, and in a few experiments staphylococcus aureus and *Bacillus coli* were injected intraperitoneally in decreasing doses into groups of white mice. Peritoneal exudate, withdrawn by capillary pipet twenty-four hours after inoculation, was examined for bacteria and cellular reaction by smears and by culturing. The result of the examination of the peritoneal exudate was taken as the criterion for comparison of the effects of various doses of bacteria, since the present study has to do with the relation of initiation of infection to dose.

Using these organisms, to which the mice were fairly resistant, it was found that as the dosage was decreased a more or less critical point was reached, below which infection failed to be initiated.

The authors discuss possible clinical bearings of this observation.

THE RELATION OF VEGETATIVE ACTIVITY OF BACTERIA TO PATHOGENICITY. AUGUSTUS R. FELTY and ARTHUR L. BLOOMFIELD, J. Exper. Med. **40**:703, 1924.

In an earlier paper, in a consideration of certain factors which seemed of importance in explaining the spread of bacterial disease, the authors suggested that the readiness with which an organism initiated infection may depend on its state of growth activity.

In the present study, the power of bacteria in various stages of growth activity to initiate infection in the peritoneal cavity of the mouse was tested. The pathogenicity of bacteria from the same culture in the stage of active growth (five or six hour cultures) and in the period of decline (from twenty-four hour to four day cultures) was thus compared.

Hemolytic streptococci and pneumococci were used. The pathogenicity, as measured by the minimum lethal dose or the size of the maximum dose of the bacteria which failed to infect, was found to be much lower in the stage of decline than in the stage of active growth.

The authors conclude that their experiments demonstrate a distinct difference between relatively young cultures of bacteria and the same strains during the period of decline as regards invasive power and pathogenicity, and that these differences must be distinguished clearly from specific alterations in virulence, such as those produced by animal passage. They stated that the exact interpretation of these observations is not perfectly clear; to what extent the results have been due to injury to the bacteria by products of culture growth it is impossible to say. At any rate, the experiments seem to bear definitely on the problem of infection, so far as they show that purely temporary modifications of growth activity, whether or not brought about by specific injury, lead to changes in invasiveness which are quite analogous to the test tube phenomenon of lag. They think it likely, on the basis of this study, that bacteria entering the upper air passages in an inactive growth phase may be disposed of before activity can be resumed, and suggest, also, the possibility that these experiments may have some bearing on the genesis of epidemics, especially as regards the preepidemic phase.

McCLURE, Evanston, Ill.

Nutrition

DIETARY FACTORS INFLUENCING CALCIUM ASSIMILATION. V. THE EFFECT OF LIGHT ON CALCIUM AND PHOSPHORUS EQUILIBRIUM IN MATURE LACTATING ANIMALS. E. B. HART, H. STEENBOCK and C. A. ELVEHJEM, J. Biol. Chem. **62**:117, 1924.

This is a study of the calcium and phosphate intake and output on two lactating goats and one dry goat, living in comparatively dark cages and receiving some deficit of vitamin A. The tendency was for the animals to develop a negative calcium balance: that is, excrete more calcium than was taken in. The lactating animals showed the negative calcium balance sooner than the nonlactating animal. When the animals received irradiation from a quartz mercury vapor lamp, the calcium balances became positive. The phosphate balance was also rendered more positive. The paper brings out the fact that the value of light in preventing osteoporosis in adult animals is similar to the value of light in preventing rickets in growing animals.

FAT-SOLUBLE VITAMINS. XX. A MODIFIED TECHNIC FOR THE DETERMINATION OF VITAMIN A. H. STEENBOCK, MARIANA T. NELSON and ARCHIE BLACK, J. Biol. Chem. **62**:275, 1924.

The authors propose a method of testing for the presence or absence of vitamin A in foods. The confusion caused by the usual concomitant absence of antirachitic vitamin is avoided by irradiating the experimental animals. Thus, hog millet and common millet were found to contain vitamin A, but to be deficient in antirachitic vitamin.

Alfalfa, which had been cured in the dark, was found to be deficient in antirachitic vitamin, but to contain vitamin A, while alfalfa which had been cured in the sun and exposed to rain, was found to contain no vitamin A, although the antirachitic vitamin was present.

FAT SOLUBLE VITAMINS. XVII. THE INDUCTION OF GROWTH-PROMOTING AND CALCIFYING PROPERTIES IN A RATION BY EXPOSURE TO ULTRAVIOLET LIGHT. H. STEENBOCK and A. BLACK, J. Biol. Chem. **61**:405, 1924.

The author's experiments were made with white rats, aged 3 weeks, which were fed a diet containing a deficiency in the antirachitic vitamin and vitamin A. Rats fed on this diet ceased to grow in about two weeks, and remained at constant weight until they showed signs of deficiency in vitamin A by appearance of ophthalmia and respiratory infections. To prolong the experiments, hog millet seed or specially treated alfalfa were added in small amounts, as they contain some vitamin A and very little of the antirachitic vitamin.

The main object of the research was to study the effect of irradiation of the diet on the growth of the rats. A Cooper-Hewitt light was used. The rats were kept in a room free from sunlight. It was found that rats receiving the irradiated diet gained in weight continuously until the end of the experiment (from four to six weeks), doing as well as animals who were themselves irradiated, while the control animals stopped growing in two weeks.

The irradiated ration was still efficacious, when heated at 96 C. for forty-five minutes, or when let stand for twenty-four hours, or when subjected to vacuum, or when the irradiation took place in a stoppered quartz or pyrex flask containing air or carbon dioxid. When the food was irradiated in a brown bottle, the rats receiving this diet showed no difference in growth from the control animals.

Using the same control diets, liver from rats which had been on this diet was added to the ration. The liver from rats which had been irradiated, and the irradiated liver of nonirradiated rats were effective in producing growth, while liver from nonirradiated rats was not growth producing. Muscle and lung tissue acted similarly to the liver.

THE EXPERIMENTAL FEEDING OF DRIED BREAST MILK. LAWRENCE WELD SMITH, J. Biol. Chem. **61**:625, 1924.

Guinea-pigs were fed a diet which would produce scurvy in fifteen to twenty days, the scurvy being preceded by a loss of weight. To this diet was added with one group of three animals fresh breast milk, with another group freshly dried breast milk, and with a third dried breast milk which had been prepared two years previously. Scurvy had not appeared in any of these animals at the end of five weeks. The guinea-pigs which were fed the old preparation of the dried breast milk did not gain in weight so satisfactorily as those receiving the freshly dried milk. The latter in turn did not gain so satisfactorily as those receiving fresh breast milk.

THE RELATION OF ARGININ AND HISTIDIN TO GROWTH. WILLIAM C. ROSE and GERALD J. COX, J. Biol. Chem. **61**:747, 1924.

White rats did not grow but lost in weight when receiving a diet in which the protein was supplied by hydrolyzed casein, from which arginin and histidin had been removed. When arginin was added to the diet, the animals did not grow but continued to lose in weight; when histidin was added, growth occurred. The quantity of histidin hydrochlorid necessary for maintenance was 0.1 gm. per 100 gm. of food (0.5 per cent. of the total protein), while 0.5 gm. (2.5 per cent. of the total protein or the proportion found in casein) caused normal growth. It appears therefore that histidin is essential to growth, and that arginin and histidin are not interchangeable in metabolism. The authors hesitate to make a sweeping deduction that arginin is not an indispensable factor in the diet, as it was impossible to tell if all the arginin had been completely removed from their hydrolyzed casein.

FAT-SOLUBLE VITAMINS. XVIII. SUNLIGHT IN ITS RELATION TO PORK PRODUCTION ON CERTAIN RESTRICTED RATIONS. H. STEENBOCK, E. B. HART and J. H. JONES, J. Biol. Chem. **61**:775, 1924.

Swine were fed a diet deficient in vitamin A. It consisted of corn, 97 parts, sodium chlorid, 1 part, calcium carbonate, 2 parts, with an allowance of centrifugated skimmed milk. One-half of the animals were kept in pens exposed to direct sunlight, while the other half were kept in relatively dark pens. In the animals studied no consistent difference in growth was found between the two groups; the animals kept in the dark pens tended to develop a condition called "rheumatism." This appears to be somewhat analogous to rickets, as was shown by the diminished phosphate of the blood serum,

diminished ash of the bone and irregularity of line of demarcation of bony tissue at the costochondral junction. Thus, sunlight appears to be a very necessary economic factor in raising of swine, especially in northern climates.

HIGGINS, Cincinnati.

IMPORTANCE OF HORMONES FOR THE PATHOGENESIS AND TREATMENT OF RICKETS. HERMANN VOLLMER, Deutsch. med. Wchnschr. **27**:901, 1924.

Vollmer treated patients with infantile rickets by means of a salve containing a variety of substances from endocrine glands. The salve was rubbed into the skin and, according to the author, healing of the rachitic bones was obtained at the end of three weeks as a result of such treatment, along with an increase of the inorganic phosphorus of the blood. These results must be looked on with considerable suspicion, since no controls were used. No evidence is offered that the diet alone was not sufficient to bring about the desired result. There is no statement as to the time of the year when the work was done, and no evidence is presented to indicate that these patients were suffering with active rickets at the time treatment was begun.

KRAMER, Baltimore.

A METHOD FOR INVESTIGATING VITAMINS IN NURSLINGS. PETENYI, Monatschr. f. Kinderh. **28**:529, 1924.

Our knowledge of vitamins comes partly from observations on sick human beings, partly from animal experiments. The results of animal experiments are generally carried over and applied to human conditions. Whether such a procedure will stand the test of time is doubtful. For this reason, Petenyl attempted to devise a method which could be applied to nurslings.

He started with the theoretic principle that growth itself might be used as an index. In this respect, nurslings due to their rapid growth make the most desirable subjects.

The scheme of experiment was to place the nurslings on a certain diet, which permitted them to thrive for a certain length of time. When gain in weight ceased, the daily quantity was increased 100 gm., with a resulting gain in weight. This procedure was repeated until an increase in quantity gave no response. The food order was either a buttermilk mixture or the Moro butter-starch-milk combination.

After two to three weeks of stationary weight, the vitamin experiment would be started, the children at that time showing symptoms much like Czerny's "Milchnahrschaden." The source of his vitamin was the potato. In twenty cases in which he proved that the results were not due to the caloric value of the potato, he was able to produce a marked gain in weight by small quantities of this vegetable, even in cases in which the quantity of the original diet had been increased 200 gm. daily with absolutely no effect.

That this vitamin was not vitamin A is proved by the fact that many of these children were on the Moro mixture. It was not vitamin B, for yeast in the diet was ineffective. Against vitamin C is the argument that there were no clinical symptoms of scurvy and that orange juice was of no value.

The writer concludes that vitamin tests can be made in nurslings, and that by this method vitamin D can be demonstrated. This vitamin may be of importance in the condition described as "Milchnahrschaden."

QUANTITATIVE CONSIDERATIONS IN THE ESTIMATE OF THE VITAMIN ACTION OF VEGETABLES. PETENYI, Monatschr. f. Kinderh. **28**:536, 1924.

The addition of potato purée to a nursling's diet in certain types of cases resulted in surprising gain. At first the writer used 100 gm., then 50, later on 30, 15, and finally in some cases only 5 gm. Of great interest and importance

is the observation that the effect of all these quantities was identical. With 5 gm. of potato purée, the gain in weight was as great as that from 100 to 200 gm. The body weight of the child, as well as the age was of no importance.

RECTAL ADMINISTRATION OF VITAMINS. PETENYI, Monatschr. f. Kinderh. **28**:540, 1924.

In studies of the vitamin contained in the potato, Petenyi experimented to see if it could be introduced into the body by rectal administration.

A suspension of equal parts of mashed potato and warm water was introduced through a rubber tube from 8 to 10 cm. in the rectum. The children retained this mixture well. The quantity of potato used daily varied from 0.5 to 15 gm. The children responded to this treatment the same as to the oral administration of the vegetable. This treatment could be used even when the stools were dyspeptic.

THE SPEED OF SEDIMENTATION OF ERYTHROCYTES IN NUTRITIONAL DISTURBANCES OF INFANTS. HILDA WOLF, Monatschr. f. Kinderh. **29**:137, 1924.

The writer finds in those cases of diarrhea without toxic symptoms no change in the speed of sedimentation. In the patients with toxic symptoms the speed was accelerated. As speed of sedimentation depends on the blood protein concentrations, she believes her observation to be another bit of evidence supporting the idea that diarrheas are of two types; one a purely local intestinal affair; the other a general affair involving the whole body and with changes in the blood proteins.

GERSTLEY, Chicago.

SOME SPECIAL CHARACTERISTICS OF WATER EXCHANGE IN THE GROWING ORGANISM. ERICH ROMINGER, München. med. Wchnschr. **71**:93, 1924.

In the evening the older child, as well as the adult, showed normal and regular concentration of the blood. The blood water during the whole period of infancy seems to be subjected apparently to irregular oscillations. The oscillations are not associated with any definite type of feeding or constitution, being present in the healthy breast fed infant just as often as in the bottle fed child. The water deposition and inhibition of the infant is intimately connected with the metabolism. The characteristic is not so much the difference in the inhibition capacity of the youthful tissues as the velocity of the inhibition. This constitutes, in the author's opinion, the most essential physiologic peculiarity of the water exchange of the growing organism.

THE VITAMIN CONTENT OF MILK FROM COWS FED ON ELECTRICALLY PRESERVED GREEN FODDER. A. ECKSTEIN and E. ROMINGER, München. med. Wchnschr. **71**:396, 1924.

The electrical preserving is done in a silo, the walls of which are made of nonconducting material, while the floor and the cover are utilized as big electrodes. The electric current is passed through the firmly packed fodder until the conductivity which in the beginning is very low does not show any marked improvement. The hay bacillus disappears and the fodder is practically free from bacteria. Ten cubic centimeters of milk from a cow fed with such fodder, prepared from corn, was shown to have sufficient supply of the necessary vitamins. Milk from such cows is considered to contain sufficient vitamin to serve for the nutrition of children.

THE RESULT OF THE FEEDING OF GOAT'S MILK TO YOUNG ANIMALS. CARL STADELMANN, München. med. Wchnschr. **71**:426, 1924.

The young of sheep, hogs, rabbits, hens, dogs, and a few wild animals reacted to the administration of goat's milk by developing diarrhea.

AMBERG, Rochester, Minn.

CONTRIBUTIONS TO THE QUESTION OF AMYLASE SECRETION IN RICKETS. J. AMBRUS, Orvosi hetil. **68**:431, 1924.

Early diagnosis of beginning rickets is important. The amylase secretion is one of the symptoms, which can easily be found in the prerachitic stage.

The conclusions of the author are:

1. The amount of pancreas amylase has increased in the urine.
2. The optimal point of amylase action depends, besides the hydrogen-ion concentration, on the kind of the cations.
3. The amylase excreted in the urine is near to molecular dispersion.
4. There is an increased amylase excretion in moist facial eczemas and in typhoid fever.

ZENTAY, St. Louis.

CONTINUED CLINICAL INVESTIGATION OF DISEASES WHICH OCCUR AS A RESULT OF FAT-SOLUBLE A DEFICIENCY. C. E. BLOCH, Ugesk. f. Læger **42**:783, 1924.

Subcutaneous injection of cod liver oil, sterilized in sealed glass tubes, has proved to be of value in the treatment of xerophthalmia in children. The first injection should be small, 0.5 c.c.; and if no idiosyncrasy manifests itself, 1 c.c. is given for four or eight days.

The author has observed that the giving of cod liver oil subcutaneously, in addition to the giving of a diet rich in fat-soluble A and cod liver oil by mouth, appears to promote the healing of corneal ulcers, xerosis and swelling of conjunctiva more rapidly than dietary treatment alone. It may be that in some instances inability to digest fat prevents the absorption of fat-soluble A to a marked degree, so that the maximum benefit is not derived from the cod liver oil when given by mouth.

The site of the subcutaneous injection is reactionless from four to eight days, after which infiltration, as well as redness, swelling and tenderness, appears. Malaise and an afternoon temperature of from 38 to 39 C. may be present for a week. The tenderness and infiltration gradually disappear over a period of weeks.

SCHLUTZ, Minneapolis.

THE DIFFERENCE IN THE VITAMIN A CONTENT OF MILK DURING DIFFERENT PERIODS OF THE YEAR. EVA SOPP, Norsk. Mag. f. Lægevidensk. **85**:123, 1924.

The author shows plainly in curves the big difference in vitamin A content of cow's milk in spring, summer and fall. For four weeks the rats are given a ratio complete in all respects, except that it does not contain any vitamin A. Then 1 c.c. of cow's milk is added to the ratio. This addition during spring from April 18 to June 9 did not have any effect on the weight curve, which was nearly horizontal during the whole period mentioned. The same addition of summer milk in the period from June 18 to July 16 gave a very good gain in weight in the rats. A gain, but not so good, was also seen during fall. The author thinks the explanation is to be sought in the way the cows are fed.

TOVERUD, Christiania, Norway.

Prenatal Conditions

A RARE CONGENITAL ANOMALY. HAROLD A. PECK, Am. J. Obst. & Gynec. **8**:761, 1924.

The author reports a case of associated hydrocephalus, spina bifida and talipes in the same infant. His survey of the literature shows only two other such cases reported.

In the discussion of the etiology of this case, he believes that most malformations in single persons are due to external influences and not to germinal defects.

ALLEN, Chicago.

Diseases of the New-Born

AN ENCLOSED BED FOR PREMATURE AND FEEBLE INFANTS. HERBERT J. W. MORGANTHALER, Am. J. Obst. & Gynec. **8**:622, 1924.

The author gives in detail a description of a portable, adaptable, and accessible crib for the protection of premature infants.

It has been used successfully at the Brooklyn Hospital for the past year and one-half.

ALLEN, Chicago.

BIRTH FRACTURE FEMUR. TRUESDELL, Bull. Lying-in Hosp. **10**:59, 1915-1916.

Six cases are reported, three due to breech extraction, two cesarean. One resuscitation is reported.

The site near or at the center of the shaft of the bone; line of fracture more or less oblique in four, transverse in two.

In every case, there was bony deformity in the form of anterior angulation.

If not treated, the angular deformities will result in curvatures, probably permanent and may exhibit unfavorable mechanical influence on ligaments. Over-riding and shortening can be ignored as well as the lateral displacements.

Treatment with splints is more practicable.

POSTERIOR DISLOCATION OF THE LOWER HUMERAL EPIPHYSIS AS A BIRTH INJURY. TRUESDELL, Bull. Lying-in Hosp. **10**:232, 1916.

Obvious birth injury is not uncommon; it is likely that many of a lesser degree escape detection. Fractures of bones are apparent, but dislocation of cartilaginous epiphyses are not shown in roentgen-ray pictures.

Three cases are reported, all of which were of version and breech extraction.

FURTHER OBSERVATIONS ON BIRTH DISLOCATIONS OF CARTILAGINOUS EPIPHYSES. TRUESDELL, Bull. Lying-in Hosp. **11**:245, 1918.

Diagnosis can be made with some assurance and verified by roentgen ray. This condition was found to be rare; fractures were near the shaft.

Two cases are reported, one humerus, two femur.

BONAR, Salt Lake City.

CEREBRAL HEMORRHAGE IN THE NEW-BORN. L. P. MACHAFFIN, Canad. M. A. J. **14**:1173, 1924.

This article is a review of the subject of cerebral hemorrhage in the new-born.

The author accepts the classification of Eustis and Munroe of Boston as the most useful classification of these cases. This divides the cases into (1) traumatic; (2) asphyxia group; (3) fetal disease group. The condition is discussed by the author from this standpoint. The main points stressed by him are:

1. Prophylaxis by careful obstetrical practice and the taking of routine coagulation and bleeding times on all new-born infants.

2. Treatment by intramuscular injection of blood and by repeated lumbar puncture to relieve pressure. Three cases are reported of children showing late effects. The neurologic findings in one of these cases is insufficient to support the diagnosis.

The article as a whole is a good review.

MOORE, Omaha.

EXTRA-PYRAMIDAL MOTOR DISTURBANCES IN SEPSIS OF THE NEWLY BORN. CORNELIA DE LANGE, Acta Pediat. **4**:60 (Oct.) 1924.

A case of low grade sepsis of the new-born is reported, terminating fatally at six weeks.

Nervous symptoms similar to those found in Wilson's disease persisted, and led the author to the conclusion that a lesion of the extrapyramidal system was present either in the lenticular nucleus, the red nucleus or the rubrospinal tract. No necropsy was obtained. In view of the fact that intense jaundice persisted throughout the course, the author thinks that the case belongs in the group designated by Schmorl as "nuclear icterus," in which the nuclei of the central nervous system shows a more intense icterus than the surrounding tissue. Presumably this excessive bile pigment injures the nerve cells directly.

HOLT, Baltimore.

Acute Infections

NOTES ON THE MOSQUITOES OF LEE COUNTY, GEORGIA. FRANCIS METCALF ROOT, Am. J. Hygiene **4**:449 (Sept.) 1924.

In this article, the author makes a study of the mosquito fauna of Lee County, Ga., and finds that *anopheles quadrimaculatus* is responsible for most of the malaria of this region. He gives a tabular outline of the different types of breeding places occurring in Lee County, together with the groups of mosquitoes which are more or less restricted to these various habitats.

EXPERIMENTAL MEASLES. I. THE THERMIC AND LEUKOCYTIC RESPONSE OF THE RABBIT TO INOCULATION WITH THE VIRUS OF MEASLES, AND THEIR VALUE AS CRITERIA OF INFECTION. JOSEPH M. SCOTT and CHARLES E. SIMON, Am. J. Hygiene **4**:559 (Sept.) 1924.

The authors here report the thermic and leukocytic responses obtained by inoculation of two series of rabbits with filtrate obtained from nasopharyngeal swabs of patients suffering from measles at different stages of development, and one series with blood, taken during the height of the eruption. In each series from 3 to 5 c.c. of sterile filtrate from the nasopharynx was injected intravenously, and a transfer was made at weekly intervals of blood taken from the heart. This was continued through twenty-four rabbits, with the interpolation in each series of one monkey as a control.

Temperature and leukocyte counts were obtained on all animals before inoculation, to serve as a basis of comparison.

The study shows that rabbits react to the intravenous introduction of the virus of measles, with marked elevation of temperature and leukopenia in practically every instance and in a characteristic manner.

Representatives of all these series of rabbits, showed the same type of response as those which have received the initial inoculation from the human being. The inoculation of the blood of these animals into monkeys produced a corresponding reaction and in addition, skin symptoms about the face.

Animals of these series, when subsequently inoculated with fresh measles blood from active human cases, showed no thermic or leukocytic reaction.

Skin symptoms were not noted in any of the unshaven rabbits.

SCOTT, Pittsburgh.

ANOMALOUS FORMS OF MEASLES. D. JESUS SARABIA Y PARDO, Pediat. Espan. **13**:255, 1924.

Measles frequently appears in atypical form. The author describes various types.

A typical eruption of measles with all the concomitant symptoms, such as coryza, lachrymation and cough, can occur without the manifestation of temperature.

Measles is sometimes associated with chickenpox. The vesicles are superimposed on the measles eruption. Both infections pursue a regular course, uninfluenced in any degree by virtue of their association.

Diphtheria may also be associated with measles. Sometimes this may prove a grave complication, but usually, especially if the tonsils only are involved, the disease will react favorably to treatment and clear up simultaneously with the measles eruption. Association of nasal diphtheria and measles is not common. Laryngeal diphtheria can occur in the early stages of measles and could account for the symptoms of croup.

Gastro-intestinal complications occur with measles. They are apt to set in about the fifth day. Vomiting is an early symptom and there is marked tympanitis.

These gastro-intestinal symptoms often usher in a septic type of measles, characterized by the persistence of irregular temperatures between 38 and 40 C. (100.4 and 104 F) and often continuing for weeks before recovery ensues.

In rare instances a hypertoxic form may occur. It is ushered in with the usual catarrhal symptoms, but with only slight faint eruption. The skin feels hot and is dry. The temperature rapidly mounts to 40 C. (104 F.). Slight convulsive movements of legs and arms occur. Respiration becomes rapid. Cyanosis supervenes with onset of generalized convulsions and the case ends fatally. The measles eruption at no stage is pronounced.

These conditions probably have bulbar lesions and lesions of other nervous centers; they are somewhat different from the malignant form which overwhelms the child in the brief space of a few days, and is accompanied by the gravest symptoms and pathologic lesions.

Recurrences or relapses in measles are not so common as is generally believed. Reports of such cases are probably largely mistaken diagnoses.

SCHLUTZ, Minneapolis.

COMBATING MEASLES INFECTION IN INFANCY. S. BUTTENWEISER, Deutsch. med. Wchnschr. **26**:876, 1924.

The author reviews the literature dealing with the use of the serum of patients convalescent from measles, for the prevention of measles. He comes to essentially the same conclusions as have been previously arrived at by others, namely, (1) that in most instances from 3 to 4 c.c. of convalescent measles' serum will prevent the development of measles in normal children as well as in the majority of those recently exposed to the disease; (2) in cases where prevention is not complete, the disease is very much attenuated in its severity and, when infection does develop, many of the classical characteristics of measles, Koplik's spots, coryza or even the characteristic rash, may be absent or, if present, be very mild. Complications during such mild attacks are rare; a fact of great importance in children's hospitals and asylums.

Protection usually lasts about from three to four months. The serum of normal adult patients who have had measles will also protect against measles when given in large doses. The author sketches a method for collecting, preserving and distributing the serum of patients convalescent from measles to be used for prophylaxis.

THE CIRCULATION IN INFECTIOUS DISEASE (ESPECIALLY IN CHILDHOOD). KRAL BENJAMIN, Deutsch. med. Wchnschr. **35**:1174, 1924.

In this article, the author gives a summary of our knowledge of the mechanism of circulatory failure in acute infections. He traces the gradual change in point of view. At first the attempt was made to localize the fault in the heart itself; "cardiac weakness" and "circulatory failure" were synonymous terms. In 1899, Romberg and Pässler showed that cardiac weakness

is not the cause of the circulatory failure produced experimentally in animals by the injection of bacterial toxins, but that it is probably due to a collapse of the peripheral vascular mechanism due to injury to the vasomotor center. This results in the incomplete filling of peripheral arterioles and a consequent fall of blood pressure. Venous stasis may be responsible for the incomplete filling of the heart and diminished cardiac output. This view was confirmed, at least so far as the heart is concerned, by the experimental work of MacCallum and that of Porter and Newburgh, although the author does not refer to the latter observers. The view that the vasomotor center is at fault was disproved by Porter and Pratt. Benjamin then refers to the more recent observations which seem to point to the capillaries as the seat of the difficulty. The work of Krogh and his co-workers on the independent activity of the capillaries of animals, dealing especially with the manner in which the supply of blood to the organs is regulated to meet functional demand, is discussed and it is pointed out that the capillaries of different organs and tissues have varying capacity for dilatation or contraction. Finally the work of Krawkow is given, showing that in normal individuals the blood vessels of the liver and kidney are capable of responding to vasoconstrictor and vasodilator drugs when perfused, even as long as two days after death, whereas the same organs, removed from patients who have died with symptoms of circulatory failure, fail to respond to such drugs even immediately after death.

The following conclusions are emphasized in this article: 1. The independence of blood pressure and pulse volume readings in acute infections, and the impossibility of determining the intensity of the injury to the circulation by measurement of the blood pressure alone; 2. Paralysis of the blood vessels in acute infections develops in two stages. During the first, the peripheral capillaries are overfilled, the pulse full and soft and often dicrotic, whereas during the latter phase the pulse is small and the capillaries of the skin contracted and partly emptied, giving rise to the well known pallor. On the other hand, the blood vessels in the splanchnic area are congested, and not infrequently this leads to swelling or enlargement of such organs as the liver or spleen which can be shown to increase progressively from hour to hour. Some prevailing notions regarding the etiology of circulatory collapse both early and late in diphtheria are discussed.

The article is exceedingly interesting but indicates clearly that there are still large gaps in our knowledge of the mechanism of the circulatory failure in acute infections.

KRAMER, Baltimore.

CONCERNING THE PROPHYLAXIS OF MEASLES. D. DREYER, Monatschr. f. Kinderh. **29**:134, 1924.

In a measles epidemic in his institution, the author was forced to use blood taken from children under 2 years of age. This proved satisfactory. He noticed also that in those children suffering with tuberculosis, the tuberculous process seemed benefited by the treatment. He suggests injecting all tuberculous children with convalescent serum even after the outbreak of the exanthem.

GERSTLEY, Chicago.

THE SYMPTOMATOLOGY OF GERMAN MEASLES. GUSTAF LINDBERG, Acta Pediat. **4**:1 (Oct.) 1924.

Lindberg observed more than 1,000 cases in a recent epidemic in Sweden. The incubation period, when it could be determined, was always between seventeen and twenty-one days. The familiar characteristics of the disease were usually found: the rash of short duration, sometimes simulating measles and sometimes scarlatiniform; glandular enlargement, particularly of the posterior cervical glands; transient fever or none; a variable exanthem, and a leukopenia with a normal differential count, except for the presence of from

1 to 2 per cent. plasma cells. Conjunctivitis was present in some cases. A strawberry tongue was not infrequently found. The only complications observed were a few cases of serous polyarthritis. The author emphasizes the great variability of the symptoms. Perhaps his most interesting observation is that the disease may occur without any exanthem. He observed several patients with transient fever, swollen glands and a typical blood picture in which he felt that the diagnosis of German measles was justified.

WHOOPING COUGH VACCINATION. ADOLPH H. MEYER, MARTIN KRISTENSEN and EINAR SÖRENSEN, Acta Pediat. **4**:21 (Oct.) 1924.

Statistics from Denmark and the Faroe Islands are given, on the effect of vaccine prepared from Bordet-Gengou bacilli. The authors doubt that the vaccine has any power to prevent or cure the disease, but they feel that attacks of whooping cough are considerably milder in vaccinated persons. The material from the Faroe Islands is particularly convincing on this point, for the disease had been absent from these islands for a number of years prior to the recent epidemic, and the population was almost uniformly susceptible. The injections were given in three doses at intervals of four days, the dose being 5, 7 and 10 billion bacilli, respectively.

Complement fixation was found regularly, reaching a maximum about eight days after the last injection. Clinical observations confirm a maximum effect at this time.

HOLT, Baltimore.

Chronic Infections

INVESTIGATIONS ON THE CONTROL OF HOOKWORM DISEASE. XXXIII. THE SIGNIFICANCE OF EGG COUNT DATA IN NECATOR AMERICANUS INFESTATIONS. NORMAN R. STOLL, Am. J. Hygiene **4**:466 (Sept.) 1924.

Detailed studies, from two persons infested with *Necator americanus* are here presented, covering periods of fifteen and forty consecutive days and show an egg output in the feces of 533,900 and 98,200 respectively.

The average of consecutive daily examination is much more accurate than single examinations.

The author states that the severity of a hookworm infestation can be fairly accurately determined by counting the eggs in the stools.

SCOTT, Pittsburgh.

SIMULTANEOUS VERNES AND WASSERMANN TESTS FOR SYPHILIS. ADELAIDE B. BAYLIS, ADELE E. SHEPLAR and WARD J. MACNEAL, Arch. Dermat. & Syph. **10**:306 (Sept.) 1924.

The authors compare the Wassermann test with the Vernes flocculation test. In general, the Wassermann is a more delicate reaction, often being positive when the Vernes reaction is doubtful or negative. The general tendency is for the two reactions to coincide. The Vernes test is considered an important check on the Wassermann and superior to other flocculation tests because of accurate control.

THE CLINICAL VALUE OF BISMUTH IN THE TREATMENT OF SYPHILIS. CHARLES H. DE T. SHIVERS, Arch. Dermat. & Syph. **10**:414 (Oct.) 1924.

The results of the treatment of sixty syphilitic patients with potassium bismuth tartrate are reported. It is advised that bismuth be used only in late syphilis, unless in the primary and secondary stages the infection has shown itself resistant to arsphenamin. Arsphenamin is superior to bismuth in the early stages. The author used from 0.1 gm. to 0.2 gm. at each intra-

muscular injection (adults) and gave an injection once each week. A full course of 2 gm. was followed by a rest of one month and was then repeated. A marked and rapid clinical effect was noted. Meningeal headaches were relieved as rapidly as with the arsenicals and often when resistant to arsenicals. The majority of those subject to arsenic dermatitis responded well to bismuth. A negative Wassermann reaction was obtained in 26 per cent. after a total of 4 gm. of bismuth salt was given. This is considered a good proportion for late syphilis.

Severe reactions are reported in three patients. These may be grouped and summarized as follows: A few hours after administration the patient may have a chill, fever, nausea and vomiting. Immediately or a little later occurs an oppression in the chest, perhaps with difficult breathing. The respirations are rapid and the pulse rate increased. The patient complains of severe pain and aching in the joints, bones and muscles. All of these symptoms may be severe for two or three days and gradually subside, the patient being free of all symptoms in from one to two weeks.

THE PRECIPITATION TEST ON SPINAL FLUID IN SYPHILIS. O. ISHII, Arch. Dermat. & Syph. **10**:442 (Oct.) 1924.

The author has found weakly positive or negative reactions in known syphilitic cerebrospinal fluids, when some of the well known precipitation tests were carried out. He describes his own modification of this test and compares the results of his modified test to those of the Wassermann reaction. A very good agreement was obtained.

THE INCIDENCE OF SYPHILIS AT THE WASHINGTON UNIVERSITY DISPENSARY AND ITS RELATIONSHIP TO ECONOMIC CONDITIONS. RICHARD S. WEISS and ADOLPH H. CONRAD, Arch. Dermat. & Syph. **10**:453 (Oct.) 1924.

The authors present data to show that there is a tide in syphilitic morbidity which ebbs and flows, and that this tide apparently is related to economic conditions. The morbidity rate varies inversely with the number of people gainfully employed in the local industrial district. This ebb and flow should be taken into account by those who are studying morbidity rates of venereal disease.

DUODENAL LAVAGE IN THE TREATMENT OF JAUNDICE COMPLICATING THE TREATMENT FOR SYPHILIS. LOUIS F. X. WILHELM, Arch. Dermat. & Syph. **10**:499 (Oct.) 1924.

Thirty of thirty-three patients recovered definitely and rapidly from jaundice and associated symptoms, following duodenal lavage with magnesium sulphate. A maximum of eight lavages and an average of two was necessary for relief.

EFFECTS OF NONSPECIFIC PROTEIN THERAPY IN SYPHILIS. SIGMUND S. GREENBAUM and CARROLL S. WRIGHT, Arch. Dermat. & Syph. **10**:551 (Nov.) 1924.

A preliminary course of six intramuscular injections of a 4 per cent. suspension of milk protein at intervals of from two to three days was followed by a series of injections of neo-arsphenamin at weekly intervals in a series of thirty-five patients. Certain varieties of the cutaneous lesions in the acute secondary cases were noted to involute rapidly, whereas in other types the eruption became extremely profuse; tertiary gummatous lesions healed rapidly. Of twenty-nine patients with latent syphilis and persistently positive Wassermann reactions, there was prompt reversal of the reaction to negative in three, while in twenty-six cases the reaction remained strongly positive even though some of the patients received fifteen injections of neo-arsphenamin.

THE WASSERMANN TEST. THE EFFECT OF INTRAMUSCULAR INJECTION OF NEO-ARSPHENAMIN ON THE WASSERMANN REACTION. DAVID L. BELDING and ROY HERBERT HOLMES, Arch. Dermat. & Syph. **10**:601 (Nov.) 1924.

Neo-arsphenamin was given intramuscularly to ten children, according to the Rosen-Fordyce technic, using a standard dose per unit of body weight. Injections were given once a week until six doses had been given. The strength of the Wassermann reaction was appreciably lowered for sixteen weeks, the period of observation. "In the 60 injections there occurred 9 instances of moderately severe pain, 5 noticeable and 2 severe indurations, and one sterile abscess, which healed in 6 weeks. Frequently the pain rendered the child restless during the first night because of the inability to lie on the side into which the injection had been made . . . although intramuscular injection can be tolerated, yet, owing to occasional difficulties, it should be used only when intravenous administration is impracticable." The authors also bring out the point that a serum, which contains a borderline quantity of Wassermann antibody, according to a standard Wassermann technic, is most readily affected by the variations in the test due to type, quality and quantity of the antigens and to fluctuating complement unit. Under such conditions it is not uncommon to get all manner of results, from a negative to a strongly positive with a single serum in repeated tests in the same laboratory or in different laboratories.

CLINICAL STUDIES ON THE KAHN REACTION FOR SYPHILIS. HARTHER L. KEIN and R. L. KAHN, Arch. Dermat. & Syph. **10**:722 (Dec.) 1924.

This paper gives the results of studies on the value of the Kahn test as a specific diagnostic agent in syphilis. The Wassermann tests for comparison were carried out in two different laboratories by different methods. The method for performing the present Kahn test is described. In hereditary syphilis, the agreement between the Kahn and Wassermann tests is very close. The Kahn test is more sensitive than the Wassermann test in treated cases of hereditary syphilis. Four weakly positive and no strongly positive Kahn tests were observed in 1,975 nonsyphilitic controls.

JEANS, Iowa City.

THE CURABILITY OF TUBERCULOUS MENINGITIS. C. FRANCIONI, Riv. di clin. Pediat. **22**:688, 1924.

The author discusses the rarity of spontaneous recovery of patients with tuberculous meningitis.

SHIPLEY, Baltimore.

THE SERODIAGNOSIS OF TUBERCULOSIS BY MEANS OF COMPLEMENT FIXATION. H. SCHLOSSBERGER, O. HARTOCH, M. LUSENA and R. PRIGGE, Deutsch. med. Wchnschr. **26**:869, 1924.

The authors studied the significance of the complement fixation reaction for the diagnosis of active tuberculosis. In a previous paper Wassermann had stated that when this reaction is carried out with an antigen consisting of human tubercle bacilli which had previously been extracted with tetralin and then mixed with a titrated lecithin emulsion, a positive reaction indicates active tuberculosis. The authors were unable to confirm this observation in spite of the fact that they not only used the original Wassermann antigen, but in addition employed other antigens of human tubercle bacilli that had been mixed with other fat solvents, such as chloroform, ethyl alcohol and acetone. Positive reactions were obtained in a large percentage of patients with active tuberculosis, but a considerable number of such patients gave negative results. Twenty-nine per cent. of definitely nontuberculous patients reacted positively.

EXPERIENCES WITH MEINICKE'S REACTION. W. LINDEN, Deutsch. med. Wchnschr. **34**:1149, 1924.

Dr. Linden made a comparative study of the Meinicke reaction and the standard Wassermann reaction for the diagnosis of syphilis. The simplicity of the former would make it clinically of great value if it could be demonstrated to be a satisfactory test. In 91.4 per cent. of clinically positive cases of syphilis, both reactions were in agreement. In 3.5 per cent. of such cases, the Meinicke reaction was positive when the Wassermann was negative. Furthermore the Meinicke reaction remained positive for a longer time following treatment than did the Wassermann. However, in sixteen cases of syphilis or 3.1 per cent. of all the cases, the Meinicke reaction was negative and the Wassermann positive. The authors, therefore, advise using both tests for diagnosis as well as in following the results of treatment.

KRAMER, Baltimore.

CONGENITAL SYPHILIS AND ANEMIA. HERBERT POGORSCHELSKY, Monatschr. f. Kinderh. **29**:6, 1924.

There has been a tradition in pediatrics that congenital syphilis itself does not influence blood morphology, but that the anemia is secondary to antisyphilitic treatment. The writer quotes a number of cases of undoubted congenital syphilis in which anemia was present before any treatment was started. Hemoglobin was as low as 45 per cent. and red cells down to 1,400,000.

GERSTLEY, Chicago.

Internal Diseases

RADIATION THERAPY IN TREATMENT OF LEUKEMIAS SUMMARIZED FROM A SERIES OF TWENTY-FIVE CASES. BERNARD F. SCHREINER and WALTER L. MATTICK, Am. J. Roentgenol. **12**:126 (Aug.) 1924.

Of these cases nine were myelogenous and sixteen lymphatic leukemia. The disease was more prevalent in the male in the proportion of four to one. The diagnosis was made by blood picture. Different concentrations of roentgen ray and radium were used in the different patients. The myelogenous type showed much better reaction to treatment than the lymphatic type.

Radiation therapy is empirical as is benzol and arsenic, but it hastens remissions of the disease with less inconvenience to the patient. The other methods may be used as adjuvants.

Radiation therapy should be used cautiously if at all in acute cases of leukemia. An optimum dose is still to be desired. No cases of cure of this disease, even with radiation therapy have been reported.

RADIATION THERAPY IN FORTY-SIX CASES OF LYMPHOGRANULOMA (HODGKIN'S DISEASE). BERNARD F. SCHREINER and WALTER L. MATTICK, Am. J. Roentgenol. **12**:133 (Aug.) 1924.

In this series, the proportion of males to females was 1.7 to 1.0 instead of the usual three to one. No amebae were found in the stools, and the histories showed no tuberculosis or malignancy as a predisposing factor. Diagnosis was generally after biopsy, tuberculous adenitis, leukemia, lymphosarcoma, Banti's disease, splenic anemia, aplastic pernicious anemia and malignancy being excluded. The attempt was made to push the dosage into the lymphogranulomatous tissue to 60 to 70 per cent. of the human erythematous dose.

Hodgkin's granuloma should be definitely diagnosed from biopsy specimens. Radiation therapy, combined with the proper medical treatment, offers the best chance of prolongation of life and palliation with least inconvenience to the patient. The medical treatment includes arsenicals. Neither radiation nor any other treatment has ever cured Hodgkin's granuloma to the knowledge of the authors.

DIFFERENTIAL DIAGNOSIS OF ENLARGED HEART AND PERICARDITIS WITH EFFUSION. C. WINFIELD PERKINS and BERTON LATTIN, Am. J. Roentgenol. **12**:171 (Aug.) 1924.

Observations were made on 350 children with cardiac disease, and especial attention was given to the acute rheumatic heart. A very large heart often indicates a rheumatic pancarditis and not necessarily a pericarditis. Pericarditis may produce an enlarged silhouette not only by effusion, but also by a chronic adhesive pericarditis. The largest hearts are produced by an acute carditis superimposed on a chronic heart disease.

The important physical signs of pericarditis with effusion are (1) signs of dry pericarditis, (2) downward displacement of left hepatic lobe (percussable), (3) actual fluid demonstrated by needle or necropsy, (4) progressive extension of flatness to the sternum, (5) extension of cardiac dulness especially to a point beyond visible or palpable apex beat and (6) signs of compression of base of left lung posteriorly. The roentgen-ray findings of the greatest help are: (1) wide shadow enveloping the great vessels at the base, (2) absence of pulsation in the left silhouette border, (3) actual demonstration of heart shadow within pericardial shadow and (4) water bottle shape of heart changing shape with posture. The roentgenogram may decide on a point of puncture.

STULIK, Chicago.

A CARDIAC INDEX FOR CARDIAC CHILDREN. J. EPSTEIN, Arch. Pediat. **41**:629, 1924.

In the study of the functions of the heart, pathologic anatomy is yielding to pathologic physiology. The cardiac arrhythmias are being studied by the use of scientific instruments of precision; the cardiac working power by the exercise tolerance tests. These exercise functional tests as performed by standard weights, while they have added a great deal to our knowledge of cardiology, do not express exactly the cardiac working capacity. Gradient efforts of moderate running, climbing stairways, walking on level ground and resting with a corresponding graded cardiac index of one, three-fourths, one-half and one-fourth will serve as a reliable and useful guide to the cardiac vital capacity. A child with a cardiac index of one requires no treatment except graduated exercises to strengthen his cardiac reserve. One with a cardiac index of three-fourths needs occasional medication and careful exercise. An index of one-half calls for a great deal of rest and digitalis, while an index of one-fourth requires the patient to be completely at rest and on digitalis treatment.

VON MEYSENBUG, New Orleans.

WHAT THE GENERAL PRACTITIONER SHOULD AND MUST KNOW ABOUT HYPERTENSION. HENRY HALPERT, M. J. & Rec. **120**:273, 1924.

With reference to blood pressure in children, Halpert states: In children, according to Melvin and Murray, the average systolic pressure is only slightly lower than in adults; the average diastolic level, on the other hand, is decidedly higher than in adults, according to these writers. By the tactile method the average systolic pressure was 105.7 in a large series of children, as compared with 108.7 in adults, while the range was 125 systolic, 84 diastolic in the latter and 132 systolic, 92 diastolic in the former. In children the relation of pulse pressure to systolic pressure was from 1 to 3, from 1 to 2.7 and from 1 to 1.6 respectively.

With regard to the variation as influenced by sex, Faber and James determined that mean systolic pressure shows no significant differences between the sexes, within the period ranging from 4 to 16 years.

According to observations made by Judson and Nicholson, in recent work of Abt, their results are not as high. They made an extensive study in well nourished children between the ages of 3 to 15. All told, 2,300 observations were made. They used the auscultatory method as introduced by Koratkoff. The systolic pressure was never as high as 105.7, except at the age of 14 years. The systolic pressure ranged from 92.0 to 99.6.

PROFUSE HEMATURIA SUCCESSFULLY TREATED BY ORAL ADMINISTRATION OF A COAGULANT PRESCRIBED FOR PATIENTS USE. M. K. WILLOUGHBY, M. J. & Rec. **120**:334, 1924.

Willoughby reports a case of moderately advanced nephritis, causing profuse hematuria, which was treated with fibrogen, a natural coagulant of the tissues isolated in accordance with the theories and technic of Mills. His results were gratifying in this particular case.

Treatment on the first day consisted of 1 c.c. of fibrogen, administered orally in ice water, on an empty stomach, three times a day; on the second day 2 c.c. of fibrogen, likewise given in ice water, twice a day; on the third day, 1 c.c. of fibrogen administered subcutaneously, before breakfast. In three days there was a complete absence of blood in the urine. This treatment is best administered on an empty stomach, when it has its normal motility.

SIGNIFICANCE OF ENLARGED GLANDS IN THE NECK. J. FRIEDMAN and S. D. GREENFIELD, M. J. & Rec. **120**:382, 1924.

The authors give a rather thorough study of these infections and sum them up as follows:

Cervical enlargements are divided into three classes, namely: 1. Inflammations; (*a*) simple adenitis following infections of the head and neck and (*b*) tuberculous. 2. Those occurring with general infections, such as: (*a*) with infectious fevers; (*b*) those conditions in which the general lymphatic system is affected with syphilis, leukemia and Hodgkin's disease. 3. Neoplasms, primary lymphosarcoma and secondary carcinoma.

In retropharyngeal glands, we look to infections of the nose and throat, particularly adenoids. In superficial cervical glands without any gross pathologic focus suspect pediculosis capitis. According to Wood, the nose and throat and mouth are regarded as the sources of cervical adenitis in 90 per cent. of the cases. The faucial tonsil is of prime importance in offering a portal of entrance to invading bacteria, principally because of the size and depth of its crypts. It offers little resistance to invading micro-organisms. In involvement of the faucial tonsil, one particular node located at the junction of the anterior border of the sternomastoid and posterior belly of the digastric, is affected. The authors have observed a condition of the cervical glands first described by Pfeiffer in 1889, called glandular fever, in which he stated that the condition was an entirely distinct condition. They have observed that their cases were preceded by some acute infection of the pharynx. They consider the small submerged fibrotic type of tonsil as the most dangerous and most likely to cause chronic adenitis.

Willis reported in his observations that in an examination of 213 tonsils removed from 108 patients, 5 per cent. showed distinct evidence of tuberculosis. This percentage agrees with observations made by others. Mitchell reports that 88 per cent. were infected with bovine tuberculosis and 12 per cent. with the human type. In summing up the infections of cervical glands these points are helpful: 1. Cervical adenitis in a patient under 2 years is likely to be simple, and not tuberculous. Over 2 years the reverse is true. 2. The family history is important as to tuberculosis. 3. Onset in pyogenic rapid. Tuber-

culous, slow, except in early infancy when the rapid onset of tuberculous adenitis is seen. In syphilis, the characteristic group involved is the posterior cervical.

KINBERGER, New Orleans.

DISCUSSION ON VISCEROPTOSIS. JOHN FRASER, Tr. Edinburgh M. J. **31**:229 (Oct.) 1924.

In discussing the subject introduced by Robert Hutchison, Fraser believes that visceroptosis has a congenital origin, as found from the abdominal viscera of children during operation at the Children's Hospital. The surgical condition of acute intussusception whether ileocecal, ileocolic, or enterocolic, occurs only when there is a congenital visceroptosis, a developmental and mechanical error existent at birth. In no other way could the ileocecal valve reach the distal portion of the colon.

Professor Russell stated that he was observing a girl, aged 12 years, who had had a congenitally narrow pyloric outlet, and who now had a large sagged stomach.

Sir Harold Stiles said that he had never seen an ileocecal intussusception in an infant who had not a prolapsed cecum and a mesentery to the ascending colon. Visceroptosis is frequently hereditary. School children of the "lanky" type have a narrow chest, sloping shoulders, wing scapulae, prominence of abdomen and extreme spinal curves. The parents of these children are often of the same build. Such children should promptly spend a year in uninterrupted physical education.

Mr. W. A. Cochrane, who has examined 3,000 chronic patients, said that for the future vitality of the race it will be necessary for the profession to insist on the right kind of physical education for the young, when most of these potential cases of visceroptosis can be prevented at their source.

NEFF, Kansas City, Mo.

CONCERNING PURPURA FULMINANS. H. BISCHOFF, Monatschr. f. Kinderh. **28**:481, 1924.

A baby, aged 20 months, had marked exudation in early infancy and had a cough for fourteen days. He awakened suddenly from sleep with diarrhea, vomiting, dyspnea and high fever. In the morning he was much worse, and hemorrhages, pinhead size, appeared all over the skin. These spread rapidly, and the child died eighteen hours after the onset.

Necropsy showed a very large thymus as well as lymphatic hyperplasia of the whole body. The thymus weighed 53 gm. Hammar gives the normal weight of this organ as 22 gm. between the second and fifth years. The writer then discusses the possibility of this having been a so-called thymic death, or whether the increased thymic secretion helped make the infection more virulent. More cases should be studied with the point of view of constitution plus infection.

LOCAL APPLICATION OF EPINEPHRIN IN GRIPPAL CROUP. W. ARNOLD, Monatschr. f. Kinderh. **28**:515, 1924.

In influenzal croup there is primarily an extreme hyperemia of the small vessels and capillaries with edema and with almost no exudative process. In view of the local effect of epinephrin on blood vessels, Arnold attempted direct application of the drug. He used a bean sized ball of cotton, saturated with from 0.5 to 1 c.c. of epinephrin, strength 1 : 1000, fastened securely to his index finger. The technic then was much like an intubation. If the pharynx were filled with mucus, it was first cleaned with sterile cotton to permit better contact for the epinephrin.

This method also is of value in the differential diagnosis against diphtheria. In the latter the treatment would be without any effect. In spite of the fact that the effect of epinephrin is instantaneous, in only one of his patients a repeated application was necessary.

CONCERNING HEPATOLIENAL SYSTEM DISEASE. F. HANAU, Monatschr. f. Kinderh. **29**:54, 1924.

In a lengthy article, the writer reports three cases of cirrhosis of the liver which do not fit into any of the usually described groups. He believes there is a constitutional background and that the condition is congenital. He believes it a mistake to consider toxic or infectious agents as the sole factors in etiology.

CONCERNING THE NEUFELD-BESREDKE SERUM INOCULATIONS FOR PREVENTING ANAPHYLAXIS. HANS FERNBACH, Monatschr. f. Kinderh. **29**:99, 1924.

This little study should be of great interest to pediatricians. Following the work of Besredke and Neufeld, physicians have believed that the injection of small amounts of serum will protect a patient from anaphylactic shock. The writer sensitized ten infants to serum and then during the period of hypersusceptibility tried intracutaneous injections of the same serum in doses of 0.1, 0.3, 0.5 and 1.0 c.c. The resulting skin reactions proved that at no time was the patient in an anti-anaphylactic state. He believes that the value of these tiny doses in the future will be not to immunize the child but to determine the degree of sensitivity. When the local reaction is at all marked, no serum should be given intravenously. Subcutaneous or intramuscular administration will be far less dangerous.

THE BLOOD PROTEIN AND UREA THERAPY IN NEPHROSIS IN CHILDREN. ALFRED EBEL, Monatschr. f. Kinderh. **29**:116, 1924.

Observations on adults have shown little change in the blood protein in cases of pure nephritis, and marked differences in conditions of so-called nephrosis. The writer reports four cases in children showing the symptoms of chronic parenchymatous nephritis. All four showed decided reduction of blood protein with increase in fibrinogen and globulin, and marked acceleration in the speed of the sedimentation of the erythrocytes. Thus a diagnosis of nephrosis may also be made in children.

Urea given in large doses proved an excellent diuretic.

GERSTLEY, Chicago.

THE TREATMENT OF INFECTIOUS DISEASES PARTICULARLY PYELITIS WITH LIVING BACTERIA. L. SAATHOFF, München. med. Wchnschr. **71**:392, 1924.

It was found that *B. coli* were killed at 52 C. after ten minutes. Freshly grown strains are killed more readily than older ones. *B. coli* killed in this manner was injected subcutaneously in small doses at first, and gradually bacteria were used which had been heated for a shorter period of time until emulsions of fresh cultures were injected. In the course of eleven years, 150 injections were made with living cultures of *B. coli* without any disagreeable accident, such as abscess formation or dissemination of the bacilli. In the most favorable cases the clinical cure and sterile urine were obtained after from four to six injections, fresh cultures being used always.

There may be a slight "Stichreaktion." Other reactions and results from injection of living *B. coli* are: (1) Local reaction with pain in the region of the kidney and the ureter; (2) rise of temperature, usually very moderate and disappearing quickly. This may serve as a guide for the next injection; (3) not infrequently immediately after the injections or after a very short rise of

temperature a more or less pronounced fall in temperature occurs; (4) from one to two days after injection, the bacteria in the urine clump together, and the leukocytes are filled with bacteria; (5) the urine becomes sterile; (6) disappearance of clinical symptoms without the urine becoming sterile. This result can only be laid to the vaccination, when the disease had lasted for a long time and disappeared rapidly after the vaccination. The results were apparently obtained in adults.

THE POSSIBILITY OF INTRA-INTESTINAL DEVELOPMENT OF OXYURIDS WITHOUT PASSAGE THROUGH THE STOMACH. NORA WUNDT, München. med. Wchnschr. **71**:546, 1924.

Twelve times, in fifty cases in which appendectomy was performed, oxyurids or their eggs were found in the appendix. The free eggs were granular, and looked exactly like those which were present in the uterus of the oxyurids in the appendix. In controlled experiments it was shown that such granular eggs did not develop under any condition, and that eggs with further developed embryos only were liberated in stomach juice of medium acidity and in physiologic sodium chlorid solution, and further that such eggs perish in the content of the duodenum, small intestine and appendix. The conclusion is reached that the appendix is a hiding place but not a breeding place of the oxyurids. Eggs of the oxyurids stand drying very well. According to the experiments of the author, it is improbable that oxyurids can develop in the intestine without passage through the stomach.

AMBERG, Rochester, Minn.

A CASE OF LIVER CIRRHOSIS IN A CHILD OF THIRTEEN YEARS. DENES SULYOK, Orvosi hetil. **68**:558, 1924.

A case of typical cirrhosis in connection with Hirschsprung's disease. The author thinks the etiology is to be found in constipation, and in toxic products due to it.

ZENTAY, St. Louis.

TREATMENT OF OXYURIASIS. T. LUZZATI, Pediatria **32**:965, 1924.

Luzzati recommends the oral administration of chloroform in the treatment of oxyuriasis. He reports excellent results in stubborn cases of this condition. Two grams of chloroform in castor oil are given in one dose. This is repeated every two weeks until no further worms or ova are noticed in the stools.

DESANCTIS, New York.

TWO CASES OF INFANTILE KALA-AZAR. ROMEO LOZANO, Arch. Españ. de Pediat. **8**:525, 1924.

The author reports two cases of kala-azar occurring in children living in villages in the province of Madrid. The children never had been near any coastal regions nor had contact with people who had lived on the coast or came from there. These cases again disprove the contention that kala-azar is a disease found only near the sea.

The specific remedy for kala-azar is antimony in the form of the tartrate, or a newer preparation (sodium acetyl *p* amino-phenyl antimonate). This preparation is dissolved in 2 c.c. of double distilled water and immediately injected intramuscularly in the gluteal region. About 3 cg. of the mixture is the initial dose. This is given every second or third day. The dose is increased progressively up to 10 cg. A larger dose is seldom necessary.

The improvement is progressive and definite under this form of treatment.

SCHLUTZ, Minneapolis.

INTESTINAL SPASM AND HIRSCHSPRUNG'S SYNDROME. IVAN BEHRING and KJ. OTTO, Acta Pediat. **4**:35 (Oct.) 1924.

A case of Hirschsprung's syndrome is reported, in which there could be felt by rectum a contraction ring at the junction of the rectum and sigmoid. Evacuations of the bowel had to be induced regularly, and at times, even when the contents of the bowel were fluid, no passage would occur unless a glass tube was passed into the sigmoid. Operation was attempted, but the child died four days later. At necropsy it was found that a button which had been swallowed had become impacted just above the constriction, setting up an inflammatory reaction with secondary cicatrization, thereby entirely preventing the relaxation of the spasm.

Similar cases of spasm causing this syndrome are reported from the literature. The usual site is at the junction of rectum and sigmoid, the so-called third sphincter. The embryology of this condition is discussed. Intestinal spasms believed to be one of several conditions which may produce Hirschsprung's syndrome.

HOLT, Baltimore.

Nervous Diseases

THERAPEUTIC FETISHISM IN PEDIATRICS. JOHN A. FOOTE, South. M. J. **17**:919, 1924.

Therapeutic fetishism or irrational prescribing is apparently still widely practiced by pediatricians. Conspicuous examples of this practice are:

1. The use of inert useless medicines.
2. The use of obsolete or undesirable preparations of an otherwise acceptable remedy.
3. The employment of a remedy of limited therapeutic application in another field where it can be of no value.

The use of the tincture of ferric chlorid is severely criticized; also the wide and indiscriminate use of calomel.

Brown mixture in combination with ammonium salts, used so extensively in pulmonary disorders, should be banished from the pharmacopeia.

The use of intestinal antiseptics and astringents comes in for much deserved criticism.

The author believes that therapeutic nihilism is really one of the most potent causes for therapeutic fetishism.

SCHLUTZ, Minneapolis.

EXPERIMENTAL STUDIES OF THE ETIOLOGY OF CHOREA MINOR. COCCHI, CESARE, Riv. di clin. Pediat. **22**:649, 1924.

Cocchi reports the cultivation of a micrococcus from the blood of four cases of chorea. In all cases, the morphologic and cultural characters were the same. Agglutination could be obtained only with serum of active or convalescent patients. Pure cultures of the organism were not pathogenic to ordinary laboratory animals, but in monkeys a condition characterized by asthenia, tremor and ataxia was produced twenty-five days after infection. Necropsy was negative, except that histologic examination demonstrated an encephalitis localized to the cortex and the region of the thalamus.

The author claims that a vaccine made from the organism has a favorable influence on the course of the disease. Some of his patients showed improvement after vaccine therapy.

The organism is a gram-positive nonmotile micrococcus, and grows readily in broth, blood, ascitic and serum agar, Loeffler's medium, etc. Not filterable. Gelatin was not liquefied nor was acid formed in broth. Milk was not coagulated. Acid was formed in glucose and saccharose, except in one case in which saccharose broth remained alkaline. Other laboratory sugars were alkaline. No gas formation was observed in any medium.

SHIPLEY, Baltimore.

THREE CASES OF SYDENHAM'S CHOREA CURED WITH NEOARSPHENAMIN. MELO, Riv. di clin. Pediat. **22**:649, 1924.

Melo reviews the various theories concerning the etiology of true chorea, and discusses extensively the several forms of management.

He, himself, rejects the supposition that chorea is due to the toxins of rheumatic infection or other bacterial disease; he disputes the idea that it is of purely nervous origin. From his observations in Mexico, he believes chorea to be a manifestation of hereditary syphilis and reports three typical cases, in all of whom syphilitic infection was demonstrated in the parents. The ages of these patients were 16, 14 and 17 years, respectively; treatment was confined to intravenous injections of neoarsphenamin, beginning with 10 to 15 cg. and gradually increasing to 1 gram, the maximum being reached in a week or ten days. Two of these patients, all of whom were girls, recovered within three weeks; the third, a case of chorea insaniens, recovered completely in four months.

AMESSE, Denver.

QUARTZ LIGHT TREATMENT OF SPASMOPHILIA IN INFANCY. H. FLESCH, Deutsch. med. Wchnschr. **46**:1577, 1924.

In this article, the author reports a series of twenty-six cases of active infantile tetany, treated with radiations from the mercury vapor quartz lamp. He comes to the same conclusions as were previously arrived at by Casparis and the reviewer, namely, that ultraviolet light is a specific for infantile tetany. Not only does it regularly cause the disappearance of all the characteristic manifestations of the disease, but corrects the underlying metabolic disturbance, namely. the associated rickets. The author of this article fails to show what relationship, if any, exists between tetany and rickets, nor why an agent that cures rickets also has a beneficial effect on tetany. No chemical determinations on the blood are reported.

KRAMER, Baltimore.

AN EXPLANATION OF THE TROUSSEAU PHENOMENON. OTTO TEZNER, Monatschr. f. Kinderh. **29**:20, 1924.

The Trousseau phenomenon results, in a case of spasmophilia, when constriction of the upper arm produces a tonic spasm which is typical of the spontaneous spasm in tetany. Numerous attempts have been made at explanation. The writer, in a considerable series of experiments on animals, believes that constriction of the arm increases the excitability of the nerve both by the direct mechanical irritation and by the resulting anemia. If this increase in excitability is sufficient when added to the increased excitability already existing in spasmophilia, a tonic spasm of the innervated muscles results, and the Trousseau sign is positive.

GERSTLEY, Chicago.

MORPHOLOGICAL AND SEROLOGICAL BLOOD STUDIES IN ACUTE AND CHRONIC STAGES OF EPIDEMIC ENCEPHALITIS. W. BERGER and UNTERSTEINER, Wien. Arch. f. inn. Med. **9**:1, 1924.

The blood picture in acute epidemic encephalitis can show pathologic changes even during the first few days of the disease. Neutrophilic leukocytosis or leukopenia is observed.

The most frequent and characteristic effect of the encephalitic infection is the production of a leukocytosis predominating in neutrophil cells. Exacerbations during any stage of the disease or any change in the condition of the patient is primarily reflected in the behavior of the neutrophilic leukocytosis.

In the active violent forms of encephalitis, the neutrophil leukocytosis is always higher than in the lethargic forms.

SCHLUTZ, Minneapolis.

POLYNEURITIS IN A CHILD: IS POLYNEURITIS DUE TO A VITAMIN DEFICIENCY? C. GRAM, Ugesk. f. Læger **46**:877, 1924.

Single instances of polyneuritis may occur in large families. Of the two cases mentioned, the one, a boy, aged 8 years, has a very extensive history in regard to the onset and gradually developing symptoms.

Before admittance to a hospital, weakness had developed to such an extent that the boy could not raise himself from a reclining position. There had been a progressive weakness of the legs extending to the arms, followed by a slight atrophy of the muscles of the involved extremities. The tendon reflexes were decreased or almost absent, but no changes were to be noticed in the cutaneous sensitivity.

The treatment of polyneuritis is a diet rich in vitamin B, cod liver oil, gentle massage of the muscles and fresh air.

One year after hospital treatment the patient was able to participate in most of the activities of childhood. No atrophy was noticeable, but there still remained a diminution of the tendon reflexes.

SCHLUTZ, Minneapolis

Diseases of the Nose and Throat

THE PREVENTION OF OPERATIVE INTERFERENCE (TRACHEOTOMY AND INTUBATION) IN THE TREATMENT OF CROUP. ARTHUR SCHLOSSMANN, Deutsch. med. Wchnschr. **28**:941, 1924.

Schlossmann argues for more conservatism in the use of tracheotomy and intubation, particularly the former, in the management of laryngeal stenosis accompanying diphtheria or so-called laryngeal croup.

In view of the fact that we possess a specific agent against diphtheria and because of the high mortality, particularly following tracheotomy, he advises the following procedure. First: the administration of a large dose of antitoxin when the patient is first seen. Second: the use of a sufficient amount of sedatives to keep the patient completely under the influence of the drug, thereby relieving the anxiety and restlessness which increase metabolism, the demand for oxygen and the production of carbonic acid. Third: the patient should be carefully wrapped and placed where he can inhale cold air.

To return to specific results, the author states that during the years 1909 to 1919, all patients with laryngeal stenosis due to diphtheria were operated on. Of these, 39.1 per cent. died. In the period represented by 1920 to 1923, 128 cases of laryngeal stenosis were observed of which 23.4 per cent. died. Of these 128 cases, thirty-six patients were operated on, of which 52.7 per cent. died, leaving ninety-two patients that in previous years would have been operated on, but were not, and of these only eleven or 11.9 per cent. died. The author concludes, therefore, that the treatment of laryngeal stenosis due to diphtheria requires, as a rule, no operative interference. Even when intubation and tracheotomy are completely avoided, the death rate from croup is always less than when such operative procedures are used to relieve air hunger. For the critical period during which the diphtheria antitoxin is developing its effect, the administration of sedatives in doses sufficient to produce rest and sleep, the admission of cold, fresh air, and the avoidance of all such factors as tend to disturb the child, are the measures recommended.

FOR AND AGAINST OPERATIVE TREATMENT OF CROUP. M. KLOTZ, Deutsch. med. Wchnschr. **46**:1576, 1924.

Schlossmann has advanced the suggestion: that the best method of saving children with laryngeal stenosis due to diphtheria is to avoid operative procedures, such as intubation or tracheotomy, relying on large doses of antitoxin along with sedatives and cool air. The validity of his conclusions was promptly questioned by Bessau and Bokay. Klotz, however, although agreeing with the

latter writers as regards the value of intubation, is of the opinion that tracheotomy is a very much abused procedure. He has never seen a child that has been tracheotomized during the first year recover, and even during the second year the mortality has been very high. After administering an adequate dose of diphtheria antitoxin and a sufficient amount of sedatives, to a patient with laryngeal stenosis, he waits twelve hours to see whether any improvement will follow. This waiting period may be increased to twenty-four hours if the stenosis is intermittent before intubation is attempted. The guide during this time is the condition of the circulation. If the cardiovascular system seems incapable of responding to the increased functional demand, intubation or tracheotomy is undertaken, even when the stenosis has lasted for a few hours. This is particularly true of children above 2 years of age.

KRAMER, Baltimore.

Diseases of the Skin

IMMUNITY IN RINGWORM INFECTIONS. SIGMUND S. GREENBAUM, Arch. Dermat. & Syph. **10**:279 (Sept.) 1924.

The author has searched unsuccessfully for a simple method of immunizing children against ringworm. Complement fixation tests showed but little development of antibodies and in but few of the cases studied. Scalp ringworm tends to undergo spontaneous cure at puberty, probably due to biochemical changes in skin secretions. It is probable that suppurative ringworm brings about a certain degree of immunity. In experimental studies with superficial ringworm, no general immunity developed, though a local immunity of at least three months' duration occurred. Reinoculation produced lesions at the exact periphery of the healed lesion. With deep infection a partial but incomplete general immunity was observed. The lesions resulting from reinoculations healed in half the time required by controls.

THE ITCH MITE AND ITS BURROW. DOUGLAS W. MONTGOMERY, Arch. Dermat. & Syph. **10**:473 (Oct.) 1924.

In discussing the peculiarities and diagnosis of scabies, Montgomery gives a good method for the definite identification of this condition: "Pinch up a fold of the skin with the burrow running along the summit of the fold, and with a scalpel shave off a slice of epidermis containing the burrow, and then lay the slice, bottom side up, in glycerin on a glass slide, place over it a cover glass and examine with a low power lens. If fortunate, and you almost always are, you will include a portion of the burrow containing possibly an itch mite, but almost assuredly eggs and feces which are equally conclusive evidence, as they are plainly visible and totally unlike anything else found in the skin."

MERCURIAL ERUPTIONS. CARROLL S. WRIGHT, Arch. Dermat. & Syph. **10**:507 (Oct.) 1924.

The author calls attention to the fact that mercury may call forth as many cutaneous reactions as arsphenamin. Mercurial eruptions may be due to an idiosyncrasy on the part of the patient, or may occur as a part of a general mercurial intoxication resulting from too prolonged use or overdosage of mercury. The prognosis is usually good with the cessation of the drug.

TREATMENT OF IVY POISONING BY RHUS TINCTURE AND ANTIGEN. CHARLES M. WILLIAMS and J. ARNOT MACGREGOR, Arch. Dermat. & Syph. **10**:515 (Oct.) 1924.

Using the method of Strickler, prompt relief was obtained in all of the twenty-six cases reported. Fifteen showed definite improvement after the

first dose. A maximum of four doses was given. No ill effects were observed. The authors believe that this is the only satisfactory means at our disposal for treating severe ivy poisoning.

JEANS, Iowa City.

TREATMENT OF ERYTHRODERMIA (LEINER) BY INTRAVENOUS BLOOD INFUSION. E. SCHIFF and W. BEYER, Monatschr. f. Kinderh. **29**:1, 1924.

The pathogenesis of the disease called by Leiner erythrodermia desquamativa is not absolutely clear. While Leiner believes it a clinical entity, Moro and Finkelstein believe that it belongs to the group of seborrheic eczema.

At any rate, the mortality is very high, averaging about 50 per cent.

The writer describes two cases in which severe anemia led to a blood transfusion. An initial injection of 45 cm. was given into the sinus, and four days later 60 cm. Both children made uneventful recoveries. The writer suggests this as a possibility of treatment.

GERSTLEY, Chicago.

Miscellaneous

DENSITY OF POPULATION AND MORTALITY IN THE UNITED STATES. THOMAS J. LEBLANC, Am. J. Hygiene **4**:501 (Sept.) 1924.

The author here reports the results of an extensive study of the influence of density of population on the mortality in the United States, using as a unit of measure the square mile. He finds that the population density in the United States for a period of years has been growing more and more, while at the same time the total death rate has been decreasing.

The exception to the above statement is to be found in the case of the death group "65 and over," which shows a higher mortality in densely populated areas. This may be accounted for by the fact that the rural districts are made up of a higher percentage of middle and old aged people while the younger and more vigorous are to be found in the cities.

In conclusion, he states that it appears from a study of registration cities that as density increases, total deaths tend to decrease.

SCOTT, Pittsburgh.

STUDIES OF THE COMPLEX NITRITOID CRISIS AFTER THE INTRAVENOUS ADMINISTRATION OF THE ARSENICALS. ISADORE ROSEN, ERNEST FRIEDRICH MÜLLER and C. N. MYERS, Arch. Dermat. & Syph. **10**:316 (Sept.) 1924.

Following intravenous arsphenamin injection, a decrease in leukocytes in blood from the finger or ear was observed in all cases. In patients showing a nitritoid crisis, this decrease was more marked and more persistent. When epinephrin was administered just preceding the arsphenamin injection, no noteworthy decrease in leukocytes was observed. It is assumed that the autonomic nervous system is stimulated by arsphenamin, producing a dilatation of the splanchnic vessels. The leukocytes migrate from the peripheral to the dilated splanchnic vessels. The change in the leukocyte count is a measure of the intensity of the reaction of the autonomic nervous system.

JEANS, Iowa City.

DECIDUOUS AND DEVELOPING TEETH. WILLIAM A. LURIE, J. Radiol. **5**:311, 1924.

Attention is directed to the importance of knowing the progress of development and age of eruption of the teeth.

Roentgenograms make it possible to observe development, and with proper knowledge interpretation is of value in the early correction of abnormal conditions. The author presents films showing normal eruption, and points out

the degree of development in the unerupted teeth shown. The confusion of infection with developing teeth can only be obviated by a knowledge of normal conditions and progress of development.

CHAMBERLAIN, Chicago.

A SIMPLIFIED METHOD FOR CAPILLARY MICROSCOPY. RUDOLF DYROFF, Deutsch. med. Wchnschr. **26**:872, 1924.

Dyroff describes a simple apparatus, by means of which it is possible to study the capillaries of the skin at the bedside.

CHENOPODIUM POISONING. R. NIEMEYER, Deutsch. med. Wchnschr. **34**:1145, 1924.

The author reports a fatal case of chenopodium poisoning. The amount administered did not exceed the usual therapeutic dose but was continued over a long time. The total amount of oil taken was 8 grams during a period of ten days. No cathartic was administered. The urinary findings resembled those found with acute nephritis and at necropsy, very extreme degeneration of the renal tubules was demonstrated. The symptoms were those of severe intoxication, prostration, fever, leukocytosis, convulsions and coma followed by respiratory paralysis. Details of the history and necropsy findings are given in the original article as well as a summary of previously reported cases.

KRAMER, Baltimore.

PROCEEDINGS OF THE DANISH PEDIATRIC SOCIETY. P. DRÜCKER, Acta Pediat. **4**:90 (Oct.) 1924.

English abstracts are given of the scientific papers, case reports and discussions of the Society for the years 1921 to 1923 inclusive.

TRANSACTIONS OF THE SWEDISH PEDIATRIC SECTION. N. MALMBERG, Acta Pediat. **4**:96 (Oct.) 1924.

Abstracts in English are given of the scientific papers, case reports and discussions of this section for the years 1922 and 1923.

PROCEEDINGS OF THE THIRD NORTHERN CONGRESS OF PEDIATRICS AT CHRISTINIA, 1924. ADOLPH H. MEYER.

Abstracts of the scientific papers, case reports and discussions are given in English. The topics include a symposium on rickets, intelligence tests in children, deficiency in vitamin A, scurvy, congenital syphilis, bloodless reduction of intussusception by taxis under anesthesia, nephritis, tuberculosis, serum treated measles in tuberculous children, insulin, relation of infection and intoxication to mineral metabolism.

HOLT, Baltimore.

Society Transactions

CENTRAL STATES PEDIATRIC SOCIETY

Minneapolis, Minn., Third Session, Oct. 31, 1924

E. J. Huenekens, M.D., *President*

A Case of Fibrous Glioma of the Left Hemisphere and Chronic Intestinal Obstruction in the Same Infant (Necropsy). Presented by Dr. F. G. Hedenstrom.

The patient was a boy, aged 17 months. The birth and development up to eight months were normal; the child was breast fed until that time. At 8 months, he had four convulsions, after which he appeared well. At 13 months he was first seen by a physician, because of a prominent abdomen and irregular stools; there was no visible peristalsis. At 15 months the patient suddenly developed twitching of the right arm and leg, followed by a right hemiplegia and unconsciousness. The child was admitted to hospital two months later and showed early optic atrophy, inability to stand, distension of the abdomen and dilatation of the superficial veins. There was paralysis of the right arm and leg, a positive Babinski and hyperactive reflexes on the right. For four weeks there was no change in the condition, when acute obstructive symptoms developed. Laparotomy and enterostomy were performed; ten days later extensive subcutaneous emphysema occurred, followed by death in forty-eight hours.

Necropsy showed distension of the intestines, and thickening and hypertrophy of the walls of the jejunum and ileum, with Y-shaped bands extending from the under surface of the liver and transverse colon, picking up the ileum and mesentery and forming almost complete obstruction of the ileum. The brain showed extensive softening of the cortical layers over one-third of the left hemisphere, with a firm mass underneath which included one-third of the left hemisphere. Microscopic section showed glial fibers and glial cells increased to four times the normal in this mass. The meninges were moderately thickened.

Spina Bifida. Presented by Dr. O. S. Wyatt.

The prognosis as regards operative mortality is about 30 per cent. Myelomeningoceles comprise 75 per cent. of all cases, and no hope is offered from operative interference; 10 per cent. of the patients have meningoceles, on which operation should be performed. Patients with spina bifida occulta should always be operated on when symptoms are present, but one should never operate if there is hydrocephalus, bilateral paraplegia, paralysis of sphincters or irreparable deformities, and operation should be delayed if possible until after the twelfth month.

Passage of Renal Stones by a Four and One-Half Months Old Infant. Presented by Dr. F. J. Schatz.

The infant was poorly nourished and had cried incessantly for five days. Urinalysis showed a specific gravity of 1.018, albumin and red and white blood cells. The blood count revealed hemoglobin 49 per cent., red blood cells 3,600,000, white blood cells 11,300. The eardrums were red and bulging. A diagnosis of double otitis media, pyelitis and secondary enterocolitis was made and myringotomy of both membrani tympani was performed. Two weeks later the infant passed five urinary calculi in a period of three days.

Following this he made a complete recovery and had had no recurrence of the attack in two years.

SARCOMA OF SUPRARENAL GLAND AND LIVER. Presented by DR. F. J. SCHATZ.

The patient was a girl, aged 2 months and poorly nourished. The family history was negative. The abdomen showed marked distension, with a palpable, rather firm and smooth mass filling the entire space between the ribs and iliac crest. The child died two weeks later and necropsy disclosed an enlarged liver, with the right suprarenal firmly adherent to the liver. The kidney and all other abdominal viscera were normal. The liver weighed 327 gm. Section showed numerous grayish nodules and the suprarenal exhibited hemorrhage throughout. Microscopic examination indicated a malignant lymphoma.

A FATAL CASE OF THRUSH INVOLVING THE SKIN, LUNGS AND NAILS. Presented by DR. JAMES TRENT CHRISTISON.

The patient was the youngest of a family of four girls. At the age of 2 years and 3 months the patient had influenza and a month later "drooling," with coated tongue and grayish-white patches covering the mucous membrane of the mouth. Thrush was diagnosed but treatment had no effect. Six months later frequent attacks of vomiting developed, with a fetid odor of the breath, and it was noted that the index finger of the left hand had become infected. Shortly afterward a spot appeared on the back of the neck, spread rapidly over the entire scalp and later involved the face. The entire left hand became involved and somewhat later the right hand. Vomiting became less frequent but a persistent cough developed. At the age of 4 years and 8 months she was suddenly taken ill with what was probably an acute exacerbation following a fresh invasion of lung tissue by the advancing thrush. A similar attack occurred nine months later. On two or three occasions, small quantities of bright red blood appeared after a severe paroxysm of coughing and the child grew gradually weaker until death occurred, three and a half years after the onset of the disease. During the entire period the laboratory findings confirmed the diagnosis. The Wassermann reaction, blood and urinary findings were always negative.

TWO CASES OF THRUSH WITH UNUSUAL SYMPTOMS AND SKIN MANIFESTATIONS. Presented by DR. FREDERICK W. SCHULTZ.

The patients were sisters, aged 6½ and 4½ years. The disease began in the older child at the age of 3 months and in the younger at 14 months. Two other children, boys, one older and one younger are well. Both patients were full term, of normal delivery and breast fed. In the older child the disease began with a dry yellow crust on the head, which was diagnosed as seborrheic eczema and treated successfully. At 6 months the mouth was involved and at 18 months the lesions appeared on the fingers, toes, dorsal surfaces and heels of both feet, the knees and elbows. At the age of 3 years this child was treated by a physician for ringworm, and all the skin lesions improved except those about the mouth. Three months later there was a general recurrence. At the age of 4 years the hair fell out but later grew again, this occurred four times in two years but the last time it did not grow again. The general development and progress of the condition in the younger child had been very similar to that of the older, and was evidently an infection transferred from the older child. The alopecia was complete. Both children were very alert mentally and had the proper mental development for their age. Both always showed marked anorexia and feeding had to be forced. There was a marked tendency to diarrhea. The diet consisted of cereals, vegetables, moderate amounts of fruit, meat once a day and either lactic acid or protein milk. Cod liver oil was given constantly. Local treatment had little effect on the lesions.

PARASITOLOGY OF THRUSH. Presented by DR. A. T. HENRICI.

The organisms from the skin lesions of the cases reported by Dr. Schlutz were unobtainable, but they were obtained from the mouth, and cultures demonstrated the typical form of the disease. The thrush organism is found in two forms, the yeastlike and the mycelial, the lesions on the body usually showing both forms. Two organisms may be confused with the thrush parasite: true yeast which is found in the mouth, probably derived from food, but this never produces mycelium. Second, the organism derived from sprue. We have tried the organism on a great number of carbohydrate mediums but it formed only acid, no gas. The organism from sprue produces both acid and gas from saccharose. The thrush organism produces an alcoholic fermentation, taking the saccharose first, fermenting it and then converting it. The thrush organism is capable of tolerating high quantities of acid. In making cultures the principal difficulty is contamination with bacteria, but if the medium is highly acid, using tartaric acid 0.5 per cent., one can completely inhibit the growth of bacteria and get a good growth of the parasite. The best procedure for identifying the organism is to inoculate the material into the medium containing agar and 0.5 per cent. acid.

TWO CASES OF CEREBRAL EDEMA OF THE NEW-BORN, ONE WITH NECROPSY REPORT. Presented by DR. W. RAY SHANNON.

Cerebral edema is a well recognized entity following brain injury in adults, but the matter of a possible traumatic cerebral edema in the new-born seems to have been largely overlooked, or insufficiently emphasized. It is characteristic of this condition that the symptoms are not immediate. The patient usually recovers from the primary unconsciousness, if this exists, which is followed some hours later by the appearance of dulness, gradually progressing into a stupor, coma and possibly death. This syndrome is met with not infrequently in the new-born, and the possibility of a developing cerebral edema should be kept constantly in mind.

CASE 1.—A boy, was born July 25, 1923, at 11:30 p. m. He was the second baby; delivery normal, except that it was necessary to induce labor by giving castor oil and quinin. The baby appeared perfectly normal for some hours but the next morning was somewhat restless and slightly cyanotic, noticeable especially in the extremities. Some slight twitchings of the extremities were noted at intervals. At 4:30 p. m. the infant was cyanotic and extremely lethargic; the respirations were irregular and shallow. The extremities were somewhat spastic but equal on the two sides. The pulse was slow and strong. No definite reaction of the pupils to light could be obtained, but a spastic downward rotation of both eyes was a prominent feature. The fontanels were not bulging but a very definite feeling of tension was noted on examining the head. A diagnosis of probable cerebral hemorrhage was made. Coagulation time was seven minutes and bleeding time three minutes. In spite of this a subcutaneous transfusion of the father's blood was given and spinal puncture was performed, and 11 c.c. of clear but yellowish-stained spinal fluid was removed under pressure. Following this, the cyanosis disappeared and the respiration assumed a normal character. The spasticity of the extremities almost cleared up, and for several hours the infant seemed to be in good condition. However, the cyanosis reappeared, together with muscular twitching and shallow, irregular respiration. A particularly severe cyanotic spell occurred at 2:00 a. m. and from this the infant never recovered.

At necropsy eight hours after death there was a definite atelectasis of the lungs, the upper left lobe only being at all well expanded. The cranial contents showed a complete absence of any hemorrhage. There was, however, a tremendous accumulation of slightly yellowish-stained fluid within the pia-arachnoid space. The brain substance was extremely edematous and soft,

and exuded a large amount of fluid on section, but the most striking feature was the tremendous accumulation of fluid in the subarachnoid spaces.

In view of the improvement which followed the release of spinal fluid pressure during the afternoon before death, it seemed that the primary pathology was the intracranial pressure, and that the atelectasis of the lungs was a secondary result of the enfeebled respiration caused thereby.

CASE 2.—A boy, was born Aug. 21, 1923. The mother was a primipara. Delivery was normal and the baby's condition did not attract attention until the third day, when the nurse noted that he was rather listless, would not nurse well, and that he had slight spells of cyanosis and twitching of the extremities. This condition continued throughout the day and the patient was seen first on the fourth day. He was well developed and nourished but extremely lethargic and could be roused only with difficulty. Cyanosis was definite, especially of the extremities. Respiration was very irregular and scarcely perceptible at times. The pulse was slow and strong. The fontanels were not bulging but the tenseness within the cranium noted in the first case was perceptible. Spasmodic turning downward of the eyes was marked. The extremities were equally spastic. Coagulation time was seven minutes and bleeding time four. A roentgenogram of the chest was negative. A spinal puncture at 10:30 a. m. obtained about 15 c.c. of a clear yellowish-stained fluid. Caffein sodium benzoate, ⅛ gr., was ordered every four hours, for its possible diuretic effect and as a respiratory stimulant. The spinal puncture was followed by very rapid improvement. At 4:30 p. m., although the infant was much improved, another spinal puncture was performed. On this occasion considerable blood was obtained, coming, probably, from the venous plexus around the dura and not from within the spinal cord. Later in the evening the spasticity of the extremities began to reappear, accompanied by twitching which at this time seemed to be more marked on the right, cyanosis and the downward turning of the eyes. A third spinal puncture was performed at 11:00 p. m. and a blood stained fluid obtained. Throughout the night the infant had occasional spells, in which he would become slightly cyanosed and twitching of the extremities would occur. At 8:00 a. m. a rather severe attack occurred, of several minutes' duration and the infant began to vomit. Coagulation and bleeding time were normal. A fourth spinal puncture was performed at 11 a. m., following which all the abnormal symptoms promptly and permanently disappeared. The infant since that time has progressed uneventfully and today is a perfectly normal baby.

This was unquestionably a case of cerebral compression. The facts that the symptoms developed so late, in the absence of a hemorrhagic diathesis, and that the first spinal fluid was entirely clear, are against its having been a hemorrhage. The bloody spinal fluid obtained later can be accounted for by failure in technic at the time of the second puncture. The effect of the caffein administration is interesting. The nurse's record contains the oft-repeated note that the baby was urinating very frequently, and it is not unreasonable to suppose that this was very definitely a factor in his recovery. Cases of cerebral edema of mild degree are probably very common in the new-born. Certainly it is not uncommon to encounter listless, sleepy babies that will not nurse well during the first few days and caffein given in such cases has surprisingly good results.

AN EXTREME CASE OF VASOMOTOR DISTURBANCE IN A TWO DAYS OLD INFANT, DUE TO INFECTION OF THE URINARY TRACT WITH COLON BACILLUS. Presented by DR. WALTER R. RAMSEY.

The baby was normal at birth and perfectly well during the first two days. On the third day the child was scarcely breathing, the skin cold and extreme cyanosis which resembled an antepartum or postpartum strangulation. All four extremities showed venous congestion in large areas, the heart beat

was feeble and respirations not over six or seven per minute. It was considered a hemorrhage case and the child was given a hypodermic injection of coagulin. Within from fifteen to twenty minutes the venous stasis disappeared, the color returned, the respiration and pulse became regular and the child seemed to be much improved. A similar attack occurred during the day but the following morning the respiration was good and the temperature 100.6 F. On examination, the urine was loaded with colon bacilli and pus. The child was put on potassium citrate and made a complete recovery. It was undoubtedly an extreme case of vasomotor disturbance due to infection with the colon bacillus.

A Determination of the Combined Ammonia and Urea Nitrogen in the Saliva. Presented by Drs. F. W. Schlutz and M. Ziegler.

Ten cubic centimeters of saliva collected without the use of a stimulant is shaken for five minutes with 2 gm. of nitrogen free kaolin and filtered. (The kaolin is prepared in quantity from Merck's kaolin by washing twice with 2 per cent. acetic, four or five times with distilled water, filtering and drying.) The filtrate usually comes through clear, but if turbid, the process is repeated. The determination of combined ammonia and urea nitrogen is carried out according to the method described in Folin's Manual for blood urea, using the aeration process for removing the ammonia.

EXPERIMENTAL RESULTS

	Subject	Urea Nitrogen in Blood, Mg. per 100 C.c.	Urea Nitrogen in Saliva, Mg. per 100 C.c.
Normal Subjects:	W. W. S.	13	12*
	W. W. S.	13	12*
	M. M.	15	10*
	M. M.	16	13*
	F. W. S.	12	13
	L. F. R.	15	15
	W. W. S.	12	13
	M. M.	13	12
Hospital Subjects:	Larson	42	27*
	Lapell	91	96
	Huncher	114	112
	Bellows	141	118

* Saliva collected by paraffin stimulation.

Bronchiectasis in Children. Presented by Drs. R. W. Morse and H. S. Lippman.

This report covers fifteen cases of bronchiectasis, which were discovered in the routine examination of 2,000 patients at the Lymanhurst School and outpatient clinic. In seven patients the history dated back for more than four years. The outstanding complaint was cough, usually not severe but aggravated by acute catarrhal attacks, which were quite frequent in seven cases. Expectoration was present in thirteen, profuse in five, but only one complained of foul sputum. The temperature varied from 99 to 101 F. One complained of night sweats; only four tired easily. Of the entire group 70 per cent. were undernourished. The Pirquet test was positive in three, the D'Espine sign in five patients; four had infected tonsils, five had dental caries and abscesses, and one had an infected maxillary sinus. Three had clubbing of the fingers.

To differentiate the pictures of early bronchiectasis from chronic bronchitis, there was the presence of irregular, scattered nodular areas of infiltration which follow the bronchi, usually going out into the costophrenic angle. The bronchial thickening was pronounced in both but did not tend to localize in bronchitis, being generally distributed. This factor will not serve as a point

of differentiation, since bronchitis and bronchiectasis usually coexist. This study showed that early bronchiectasis is very difficult to diagnose clinically, but in a child, whenever there is a history of pulmonary involvement lasting for several years, bronchiectasis should be strongly considered.

REPORT OF FIFTY CASES IN A PRESCHOOL CLINIC, WITH SPECIAL REFERENCE TO TREATMENT AND PROGNOSIS OF HABIT FORMATION. Presented by DR. E. J. HUENEKENS.

The solution of this problem is the combination of the two types of clinics, that which considers chiefly the physical aspects and the so-called "habit clinics," and that such work should be in charge of a pediatrician who has a broader view of the child than the narrower specialists, such as psychiatrists. These clinics should be premental hygiene, prechild guidance, and parents should be educated to prevent the ultimate delinquency of the child. The principal bad habit of the preschool child is anorexia, and this is of great importance in the future mental and moral development of the child, but not easy of attack. The cooperation of the senior students in the Home Economics School of Agriculture was obtained, and they visit the homes of these children and get some education across to the mothers, which is the best solution of this problem. The second method of attack is by books which are written in a simple way and which are lent to parents, and a pamphlet which has been prepared which takes up the simple problems of child training. Many of the children seem hopeless because the parents are the type who cannot carry out the things they are asked to do, either because of lack of intelligence or of will power.

A STUDY OF THE OCCURRENCE OF PEPTID NITROGEN IN THE BLOOD WITH ESPECIAL REFERENCE TO THE REST NITROGEN. Presented by DR. WILLIAM W. SWANSON.

The most complete analysis of the substances containing nitrogen in tungstic acid blood filtrates does not account for more than from 60 to 80 per cent. of the total nonprotein nitrogen. The unaccounted for fraction of nitrogen has been designated in the literature as the "Undetermined Rest-Nitrogen," which does not in any sense describe the nature of the substance containing the nitrogen.

A study of tungstic acid blood filtrates therefore was made according to the following method: 10 c.c. of tungstic acid blood filtrate, to which 10 c.c. of a saturated solution (room temperature) of barium hydroxid had been added, were boiled gently for from twenty to twenty-four hours. The solution was then concentrated to 5 c.c., sufficient sulphuric acid added to precipitate the barium and the solution made up to 25 c.c. and filtered. On the filtrate thus obtained, a determination for free and hydrolysed amino-acids was made according to Folin's[1] method. The results obtained by these methods are shown in the table. The increased amino-acid nitrogen accounted for after hydrolysis is listed under peptid nitrogen.

COLON BACILLUS MENINGITIS IN THE NEW-BORN. REPORT OF A CASE. Presented by DRS. O. W. ROWE and C. O. KOHLBRY.

The report covers a case of colon bacillus meningitis in an infant, aged 5 days. Erysipelas starting at the genitalia appeared as a coincident infection, but the point of entry of either infection was not found. It was considered likely that the meningitis had its origin from a slight skin abrasion of the rectum, or as a hematogenic infection from the intestinal tract, as suggested in the work of Cooke and Bell. The erysipelas probably started from a minute abrasion of the vulva. No necropsy was obtained.

1. Folin, O.: J. Biol. Chem. **51**:377, 1922.

ACRODYNIA: REPORT OF CASE. Presented by DRS. F. C. RODDA and JOHN BUTLER.

The case was a typical one of acrodynia. The patient made a rapid recovery following removal of the tonsils and adenoids, which were the focus of infection.

Dr. Butler showed a series of lantern slides of several typical cases.

DISCUSSION

DR. BUTLER: So far as I know, no biopsy has ever been made of the skin in these cases, but this section shows the normal skin with intense hyperkeratosis and very pronounced edema. The term "acrodynia" is wrong and should not be applied to these cases. They are in no way connected with this disease, an epidemic of which occurred among adults in France nearly one hundred years ago. It is better described as erythredema, as suggested by Swift in 1914.

Nonprotein Nitrogen Determinations Per Hundred Cubic Centimeters of Whole Blood

	Total Non-protein Nitrogen, Mg.	Urea Nitrogen, Mg.	Preformed Creatinin Nitrogen, Mg.	Total Creatinin Nitrogen, Mg.	Uric Acid Nitrogen, Mg.	Amino-Acid Nitrogen, Mg.	Undetermined Rest Nitrogen, Mg.	Peptid Nitrogen, Mg.	Peptid nitrogen per Cent. of Undetermined Rest Nitrogen
Normal									
1	29.0	13.0	0.5	1.6	0.9	8.7	4.8	4.3	90
2	38.0	17.0	0.76	1.5	0.84	7.0	11.76	11.0	93
3	45.0	17.8	0.8	2.0	0.88	8.7	15.6	11.0	70
4	42.0	11.0	...	...	...	8.0	23.0	20.0	..
5	40.0	17.0	...	...	...	8.3	14.7	13.3	..
6	40.0	13.8	...	...	...	7.8	18.4	13.0	..
7	43.0	16.5	...	...	...	7.8	19.0	15.0	..
8	36.0	17.6	...	...	...	9.1	9.3	5.2	..
9	41.5	14.0	...	..	...	8.7	18.8	11.3	..
Pathologic									
10	142.0	108.0	1.8	4.6	1.7	8.7	19.0	13.8	72
11	114.0	91.0	...	...	...	8.0	15.0	7.0	..
12	115.0	90.0	...	...	1.6	7.0	16.4	14.0	..
13	150.0	114.0	3.0	...	2.0	7.7	23.3	20.0	..
14	154.0	120.0	...	3.2	2.6	7.3	21.0	16.0	76

DR. J. G. BILDERBACK: I agree with Dr. Butler that the disease is badly named in this country and that erythredema is much better. During the last year Patterson of London obtained a necropsy on a patient who died of an intercurrent disease, and found that the disease affected particularly the peripheral part, the sensory nerves more than the motor. The difficulty these patients have in moving about evidently is due to muscular weakness rather than to paralysis. In all of my patients except one there was absence of the kneejerk, but in the one exception the kneejerk was more marked than in any disease I have ever seen. This child was older than the average patient of this type and described peculiar sensations in the legs and palms.

REPORT OF CASE OF EXTENSIVE CONGENITAL DEFECT IN THE SKIN IN THE NEWBORN INFANT. Presented by DRS. F. L. ADAIR and C. A. STEWART.

The patient was the third child; all the others were normal. The mother gave a history of obstruction during pregnancy, and at birth there was a band of translucent membrane which extended across the umbilicus of the child to either side of the body and down to the crest of the ilium, up to the axillary fold. There was also a small area on the thigh and another on one shoulder. Scars connected these areas, which indicated that the condition had been more extensive in utero. Treatment consisted of dusting powder,

covered with gauze soaked in paraffin to prevent sticking. The lesion healed spontaneously and completely in about five months, and left very little scarring.

HUNGER DYSPEPSIA, WITH REPORT OF TWO CASES. Presented by DR. C. R. MORIARTY.

This is a report of two undernourished children, aged 12 and 23 months respectively, both of whom showed extreme irritability and persistent diarrhea. Increased and correctly regulated diet brought rapid gain in weight, properly formed stools and permanent recovery.

A CASE OF EXTREME OBSTRUCTIVE DYSPNEA WITH POSSIBLE ACUTE THYMIC ENLARGEMENT. Presented by DR. EDWARD DYER ANDERSON.

The child was always underweight and eczematous, and when several weeks old developed difficulty in breathing, with definite symptoms of obstruction. When first seen the child was fighting for breath and cyanotic, with a temperature of 101 F. Cultures were negative and there was no history of foreign body. Roentgen-ray examination showed nothing except questionable enlargement of the thymus. Bronchoscopy was done and revealed nothing, but on introduction of the bronchoscope the condition of the child immediately improved and it breathed without difficulty. Intubation was decided on, but with the tube in place the labored breathing recurred, which indicated an obstruction between the larynx and the bifurcation of the bronchi. The temperature was 103.5 F., leukocytosis 23,000. It was decided the condition might be due to some acute infectious process and roentgen-ray therapy was used. Soon after the use of the roentgen ray, there was a convulsion which lasted about five minutes, but within twenty hours the child was markedly improved, made a perfect recovery and is now entirely well. The acute obstruction was probably due to an enlarged thymus, which was improved by roentgen-ray therapy.

ANEMIAS OF INFANCY. Presented by DR. H. S. LIPPMAN.

Analysis of cases studied during the last three years shows that anemias of infancy and childhood can be classified into three groups, depending on the reaction of the blood-forming organs. In Group 1 are the anemias associated with hemorrhage, pyogenic infections, acute infectious diseases, hemolytic icterus and the so-called von Jaksch disease, which is not a specific blood disease. These anemias are due to destruction or loss of red blood cells and hemoglobin faster than they can be produced by the blood-forming organs.

In Group 2 we see evidences of diminished activity of the hematopoietic apparatus, which fails to produce the normal supply of red blood cells and hemoglobin. This occurs to a lesser degree in measles, influenza and typhoid and to a more marked degree in chlorosis associated with nutritional disturbances. In the group of hypoplastic anemias, the leukopenia is usually associated with a relative lymphocytosis.

In Group 3, the blood-forming organs are so burdened with the production of abnormal cells that the supply of red blood cells and hemoglobin suffers and anemia results. Of these malignant conditions, acute lymphatic leukemia most commonly occurs in early life.

GROWTH IN THE FIRST YEAR. Presented by DR. L. F. RICHDORF.

About 600 normal, full term babies were measured, twenty-five boys and twenty-five girls in each month of the first year. From this study it was determined that during the first year the increase in height is about 10 cm., one-fourth of which is in the head and neck; one-fourth in the chest and abdomen and one-half in the lower extremities. Practically all measurements

except the length of extremities increased most rapidly in the first three months, the extremities showing the most increase between two and a half and five and a half. It was apparent that growth in length is determined somewhat by the type of feeding, that measurements reveal the sequence and extent of growth, and that a study of both length and circumference is necessary. The principal growth in the first year, particularly after the third month, is in the length of the lower extremities and this measurement gives a fairly good index to past nutrition and present development.

ECZEMA IN BREAST FED BABIES. Presented by DR. W. RAY SHANNON.

Eczema in breast fed babies is dependent on an underlying allergic condition to foods transmitted to the infant through the mother's milk. In a series of carefully studied cases it has been found that eczema in breast fed babies could frequently be cured, and almost always helped by the elimination of those foods from the diet of the mother to which sensitization can be demonstrated in the baby by the cutaneous protein test.

LIPODYSTROPHIA PROGRESSIVA SUPERIOR. Presented by DR. T. L. BIRNBERG.

The patient was a girl, aged 4 years, whose family history was negative. The emaciation began at about the sixth month. Multiple skin lesions and intraorbital edema were present since birth; there was spasticity of the lower extremities and constipation. From the umbilicus downward the body was normal, but the emaciation of the upper portion was progressive and cod liver oil and forced feeding had no effect. The child was subnormal mentally. The Wassermann and Pirquet reactions were negative; bleeding and clotting time were normal.

URTICARIA PIGMENTOSA: INFANTILISMUS. Presented by DR. T. L. BIRNBERG.

The patient was an under-developed child, aged 6½ years, who was apparently normal mentally, but the speech was slightly abnormal. There was pleuriglandular disturbance and marked evidence of Addison's disease. Suprarenal extract was of much assistance when first given but of no permanent value.

PNEUMOTHORAX. Presented by DR. T. L. BIRNBERG.

This patient was under observation for about eleven months. She was well until about 1 year old, and since then she has had frequent colds and loss of appetite but no sweats or fever. This probably was a case of complete pneumothorax originating in early infancy, with consequent lack of lung development.

VALUE OF PHARYNGEAL AND LARYNGEAL SUCTION IN TREATMENT OF SPECIFIC INFECTIOUS DISEASES (WITH LANTERN SLIDES). Presented by DR. E. S. PLATOU.

The necessity for intubation has diminished from 30 to 50 per cent. since this method came into use two years ago at the Willard Parker Hospital. Ordinarily, two or three times is all that is necessary, but occasionally it must be used five or six times before the membrane is removed. If severe edema is present it will not relieve the condition. The method can be used by anyone who can use a laryngoscope.

POSSIBLE ANATOMIC BASIS FOR CERTAIN GASTRO-INTESTINAL SYMPTOMS OF INFANCY. STRANGULATED HERNIA. Presented by DR. PLATOU.

The obstinacy of some cases of "colic," in spite of all palliative measures, suggests an anatomic basis as a possible explanation. A girl, aged 8 weeks, had a tendency to constipation and in spite of all treatment continued to have

severe "colic," characterized by extreme restlessness, eructation and abdominal distension which was frequently relieved only by enemas. During a bath the mother noticed a swelling the size of a hazel-nut in the left labia. There had been no bowel movement for forty-eight hours and the child was extremely irritable. A diagnosis of strangulated left inguinal hernia was made. Operation was performed at once and a very dark blue sac was found, which contained a piece of bowel, the left ovary and tube, and which was strangulated by the internal ring. The child made an uneventful recovery and since then has had no recurrence of gastro-intestinal symptoms.

REPORT ON ONE CHILD FED WITH CONCENTRATED FEEDING. Presented by DR. B. ROSENHOLTZ.

The report covers the case of a child who had a typical pylorospasm, with projectile vomiting. The mother refused operation. The child was placed on thick gruel feeding but lost 8 ounces in five days. The Hess method of duodenal tube feeding was then resorted to, the first feeding taking one hour and twenty minutes. This was used three times a day for two weeks, giving 2 ounces of mother's milk, a teaspoon of sugar, and giving about fifty calories to the kilogram of body weight. The child retained everything given and the stools became good. On the fourteenth day, one duodenal feeding was omitted and the Broeck feeder used. The baby left the hospital six months later, weighing 9 pounds and 1 ounce (283 gm.). The child would not take cereals and developed anemia, so whole blood and later citrated blood was used intraperitoneally. The hemoglobin increased from 22 to 77 per cent. and the child is now walking.

ACUTE OTITIS MEDIA IN INFANTS AND CHILDREN. Presented by DR. ROY ANDREWS.

The symptoms of acute otitis media are so vague and the cases so numerous that every infant and child with a temperature, or with any of the exanthems or influenza should have a careful and repeated otoscopic examination. If these conditions are diagnosed and properly treated, there will be less catarrh of the middle ear, impaired hearing and mastoid infection.

FOUR CASES OF OSTEOGENESIS IMPERFECTA. Presented by DR. ALEXANDER STEWART.

CASE 1.—The child, aged 5 years whose family history was negative, was breast fed. The illness started at the age of 4 months with a fracture of the right humerus. Four fractures occurred within the next year and the condition had persisted, thirty-two definite fractures being noted. One occurred from turning over in bed. Phosphorus, cod liver oil and heliotherapy gave no results.

CASE 2.—A youth, aged 19 years, had never walked. The disease started when an infant and the deformity of the legs increased. The pelvis was interesting because of a megalocolon and the very small outlet, the pubes and symphysis being very close together, with only an opening of 1.6 inches. There had been no recent fractures, but the deformity was marked and treatment had been without avail.

CASE 3.—A girl, aged 9 years, a sister of the patient referred to as Case 2. This child never walked very well, but the first fracture occurred when she was 8 years old, several fractures following since then.

CASE 4.—The patient, aged 16 years, was typical, except that the skull was unusually thick.

The blood chemistry and blood analysis had been done on all the patients, and had shown no changes in the phosphorus or calcium content. The urea and nonprotein nitrogen were within normal limits. Everything advised in

the treatment of such conditions has been tried, but the deformity seems to progress in all the cases and fractures continue to occur.

SCLERODERMA. Presented by DR. GLENN R. MATCHAN.

This case represented the fibrous type of scleroderma. The child was aged 7 years. The mother noticed the first lesion on the right leg in 1923 and the condition had been progressive, apparently following acute infection of the tonsils and adenoids. The patient complained of inability to flex the leg and of discomfort in the sartorious in flexion of the abdomen. There was a moderate degree of anemia and a slight increase in temperature.

OSTEITIS FIBROSA CYSTICA. Presented by DR. THOMAS MYERS.

This patient was a girl, aged 9 years. Birth was normal and she was breast fed until 11 months old. The joints have been painful and swollen probably since birth. When 4 months old, the left wrist was noticeably swollen and tender and painful swellings had occurred, sometimes as often as every week, in nearly every joint. The child was never able to walk nor stand. She sat up at 1 year but since then had improved and grown very slowly. The lower jaw was straightened out with a deformity at each angle. She was pigeon-breasted; there were marked deformities of all epiphyses, marked thickening, contraction of hip and knee joint and of left hand. There was kyphoscoliosis, marked muscular atrophy and adductor spasm. A roentgen-ray examination showed that the joints were apparently normal, the fractures occurring principally in the epiphyses or in the diaphyses near the junction of the epiphyses. There was marked enlargement with cystic changes of the ends of the long bones. There were no apparent fractures of the shafts and they were not lacking in calcium but were small in caliber. The cortical layer was normal.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Nov. 16, 1924

The Children's Memorial Hospital, Chicago

JOSEPH BRENNEMANN, M.D., *Chairman*

CONGENITAL TUMOR OF KIDNEY. Presented by DR. A. H. MONTGOMERY.

This was a case of a congenital kidney tumor of the mixed cell type, in a baby, aged 20 months. Operation was advised and performed with subsequent recovery of the child.

OSTEITIS FIBROSA CYSTICA. Presented by DR. A. H. MONTGOMERY.

The patient was a child, aged 7 years, who was brought to the hospital one year ago because of a fracture of the upper portion of the humerus. Roentgen-ray examination showed a large elliptical area, with a trabecula in the surgical neck of the bone. There was a very definite line of fracture passing through this area. No operative treatment was used but a splint was applied. A roentgen-ray picture taken six months later showed that the fracture had healed and that the cyst area was filling with normal bone. Dr. Montgomery expressed the opinion that the condition would continue to improve and that the bone would return to a normal structure within two or three years. He showed a roentgen-ray picture of another patient, on whom he had performed an open operation because the cyst did not heal, although the fracture healed under simple splint treatment. The operative

procedure consisted of crushing in the wall of the cyst and pushing the fragments of bone into the cyst cavity, thereby producing an osteogenetic process which had gone on and produced good bone. The child had had no further difficulty with the bone cyst. Several other roentgen-ray pictures were shown, and the differential diagnosis between bone cysts and sarcoma, tuberculosis, syphilis and osteomyelitis was outlined.

ECZEMA. Presented by DR. F. J. CORPER.

The literature of recent years contains numerous articles concerning the treatment of infantile eczema, based on the information obtained from protein sensitization tests. The encouraging results obtained by various authors have led to the common belief that the problem of treating such conditions has been solved. That results contradictory to positive cutaneous tests may sometimes be obtained was illustrated by the following two cases.

CASE 1.—The first patient was a child, aged 14 months, who exhibited positive tests to egg and wheat globulin. This patient showed improvement only when placed on a diet of dried milk. Wheat was eliminated from the dietary for several weeks without any change in the skin manifestations, and egg had never been ingested except possibly through the mother's milk. The two marked positive tests appearing on the back were due to egg and wheat globulin. At the time of presentation, the baby was receiving dried milk and a large amount of food daily containing wheat. The eczema had entirely disappeared, although the ingestion of egg apparently caused some return of symptoms.

CASE 2.—This baby, aged 10 months, had suffered from eczema from the age of 3 months. The child had been artificially fed almost from birth, and was found positive to egg white and wheat only, all other tests being negative. No improvement was noted on an egg and wheat free diet, and the skin manifestations subsided only after the feeding was changed to albumin milk. There was no history of the ingestion of egg. After improvement had occurred, wheat cereals were added to the dietary with no exacerbation of eczema and at the time of presentation the infant was receiving a large amount of wheat daily.

DERMATITIS HERPETIFORMIS. Presented by DR. E. A. OLIVER.

The patient was a child, aged 7 years, with a skin eruption which had been present for nine weeks, consisting of papules, vesicles and bullae, all three being present at the same time on some occasions. The lesions were absolutely symmetrical, both hands and feet and buttocks being affected.

Two previous patients and this patient had received arsenical therapy. The condition of the two previous patients had cleared up and this patient showed marked improvement.

GLIOMA OF THE EYES. Presented by DR. H. A. ROSENBAUM.

The patient was an infant, aged 9 months, who had never been able to sit up. Examination showed that the child was spastic, with increased reflexes, nystagmus of the right eye, and an opacity which apparently was deeper than a cataract, and which reached almost to the cornea. The Wassermann reactions on the infant and the mother were negative.

The comment of Fuchs that in glioma of the eye an inferior physical background is often present seemed to be true in this case.

CYSTIC HYGROMA. Presented by DR. J. L. REICHERT.

The patient was a child, aged 15 months, who was normal at birth except for a soft, compressible mass about the size of an orange over the left buttock. The anus was drawn up out of the normal position but was normal in shape. A definite impulse was transmitted to the mass when the child strained. There

was an indefinite mass in the abdomen which extended above the brim of the pelvis, which also showed an impulse when the child strained. The external mass transilluminated light.

On barium roentgen-ray examination, it was seen that the rectum, sigmoid and colon were normal and the bony pelvis was complete. Spina bifida was ruled out because there was no demonstrable connection between the mass and the cerebrospinal canal. The roentgenogram revealed no solid material in the mass, which ruled out the dermoid cyst, and there was no intestine included in the mass so that it was obviously not a hernia. The idea of its being lymphatic was emphasized by the fact that it transmitted light very readily, and the diagnosis of cystic hygroma, hypertrophy and cavernous dilatation of the retroperitoneal and perirectal lymphatics was made.

The parents refused operation so the child was given radium therapy, and had received five doses, averaging 300 mg. for two hours at a distance of 3 inches. The mass had become much smaller but the intra-abdominal mass became more firm and the size of a child's thumb. The parents then left town and the child was not seen for some time, but they said that the mass remained stationary in size until about four weeks before presentation, when it started to grow very rapidly. At the time of presentation it was 15 cm. in circumference and 35 cm. long. The anus was then pulled up into the mass and into a slit about 5 cm., long and the mass was no longer transillumined by light. It was hot, tender and red and the child had a temperature of 101 to 102 F. with 40,000 leukocytes, 50 per cent. lymphocytes, and it was decided to drain the mass. A needle was inserted and 750 c.c. of sterile material was withdrawn. On standing, this separated into three layers, the lower one of which showed nothing but cellular débris, a middle layer made up principally of red blood cells and a third layer made up of large and small lymphocytes. At no time had there been any disturbance of bowel function, but the prognosis was thought to be bad.

MULTIPLE CONGENITAL CONTRACTURES. Presented by DRS. B. H. MOORE and E. J. BERKHEISER.

The patient was a child, aged 14 months, who had congenital club feet, some contraction of the knees, flexion contraction of the hips, contraction of the wrist and fingers. The elbows were fairly normal, shoulders fairly free in motion. There was slight webbing of the fingers, a saddle nose and a somewhat contracted back, and bilateral ptosis of upper eyelids. The child showed practically no flexibility but was stiff and rigid. The muscles were poorly developed and the skin was thick. There was no known etiology in the case. The blood Wassermann was negative. Roentgen-ray examination showed no evidence of spina bifida occulta.

An attempt was to be made to straighten the child by means of casts.

CONGENITAL DISLOCATION OF HIP IN NEGRO. Presented by DRS. B. H. MOORE and E. J. BERKHEISER.

The patient was a negro, aged 8 years. Roentgen-ray examination showed dislocation of the hip.

Examination also showed an interesting condition about the head and neck, although the child had not complained of pain in that locality. There was a kyphosis and some rigidity of the neck, and a diagnosis was made of Pott's disease in the neck but roentgen-ray examination showed a dislocation instead of Pott's disease.

SPRENGEL'S SHOULDER (BILATERAL). Presented by DRS. B. H. MOORE and E. J. BERKHEISER.

The patient was a boy, aged 2 years. On examination, there was very evident shortening of the neck which was clearly due to elevation of the

scapulae, shortness and contraction of the muscles in the posterior portion of the neck. The child was unable to lift his arms completely and the scapulae were quite well fixed.

Roentgen-ray examination showed the scapula elevated far up in the neck as contrasted with the normal position. The condition was bilateral, contrary to the usual findings.

A Case of Unknown Diagnosis. Presented by Dr. Joseph Brennemann.

The patient was a girl, aged 5 years, who presented a skin disorder of four years' duration. It began with a scaling eruption on the scalp and forehead which was treated for eczema. The child was first seen in the Hospital two years previously, at which time she was undersized and quite unhappy, often rubbing her hands and feet together, evidently because of itching. At the time of presentation there was a crusted lesion on the lip, with deep fissures between but no apparent destruction of tissue. On the palmar surface of the hand was a peculiar, well defined lesion. When the child was admitted she was covered with the same sort of crusted lesions as appeared on the lip, on both palms and soles and about the mouth. The nails showed trophic disturbance and most of them had been picked off. The fingers were somewhat swollen and there was some contraction due to the lesions. There was no generalized sweating and no redness. The left foot was not as much involved as the right. The skin was thickened and could be removed in thick lamellae. The toenails showed trophic disturbance, and the destruction of the tissue of the feet was more marked than that of the hands. There was no marked insomnia and the unhappiness was not thought to be pronounced, as in acrodynia, but the child had not improved since she had been in the hospital. About the anus was a funnel-shaped crater, rather gray in the center with the edges coapting perfectly.

They had first considered the condition some sort of a trophic disturbance. One physician thought it might be a case of impetigo but the lesions were not typical and there had been no improvement. Thrush organisms had been looked for but none were found. The child was presented before the Chicago Dermatological Society, and the diagnosis of erythredema, or acrodynia, was considered the most likely, although few of the symptoms of this disorder were present and the duration was unusually long. This child had lost no teeth and there was no wasting of the muscles such as usually occurs.

The child was being treated with ammoniated mercury ointment and Fowler's solution but had made no improvement, and Dr. Brennemann thought it might be well to try wet dressings, rather than salves, with the idea that it might be an infection.

DISCUSSION

Dr. Oliver said that a definite diagnosis of erythredema was not made, although several of the members of the Dermatological Society thought this the most probable diagnosis. So few cases of this disorder have been seen that it was thought they might have all been of the acute type and there was no reason why there might not be a chronic form.

Dr. Abt asked if they had considered syringomyelia as a diagnosis.

Intestinal Obstruction (?). Presented by Dr. Charles Schott.

The patient was a child, who was first seen on the preceding day. There was a history of diarrhea and vomiting, with increase in the size of the abdomen and generalized pain preceding these attacks. The vomitus consisted of large amounts of dark fecal material. Examination showed a tremendous peristaltic wave, hemoglobin 80 per cent., 4,500,000 red cells and 7,100 white. The Pirquet test was negative. Roentgen-ray examination, following a barium enema six hours before, showed the barium in the ascending colon. There

was no definite evidence of tumor and the differential diagnosis would have to consider tuberculosis, adhesions, remnants of the urachus and Meckel's diverticula. The mouth was not sore.

UNRESOLVED PNEUMONIA. Presented by DR. CHARLES SCHOTT.

The patient was a boy, with complete flatness of the left chest with no heart dulness. The entire left lobe was involved, and the heart was so pulled in that the condition was believed to be either a collapse of the lung or some nontuberculous inflammation. Roentgen-ray examination showed no shadow to the right and there was nothing found on percussion. There was a scoliosis to the affected side, and in a similar case the same findings had been recorded. Roentgenograms of both patients were presented.

HEART DISEASE. Presented by DR. HAROLD A. BACHMANN.

Dr Bachmann said that during the last seven months, there had been two interesting series of cases in the heart ward. The first series, consisting of seven or eight patients, was admitted the last of April and first of May. All were typical cases of pericarditis. Five showed evidences of heart failure. These patients were in poor condition on admission and went from bad to worse, regardless of the treatment instituted and succumbed to the disease. The second series of cases which was now under observation presented symptoms much like the former group, except that no pericarditis was present. Symptoms of heart failure were present, with edema, rapid pulse, large liver and two had had fluid in the right chest. This series of cases, in contradistinction to those in the earlier series, had responded very nicely to treatment, which was thought to be of considerable diagnostic importance.

Previous to the death of one of the patients, they had made a very elaborate diagnosis of the valves which they thought would be involved, but necropsy showed an adhesive pericarditis with no valvular changes to account for the murmurs. In another patient the adhesions were not well formed; a definite pericarditis was present, but again with no evidence of vegetations on the valves. A third patient showed some evidence of vegetations on the mitral leaflet, but they were small and recent and could not have been responsible for the murmurs that were heard, which emphasized the fact that one must be extremely careful in making a valvular diagnosis, in the presence of pericarditis. In all three of the cases the valves were almost intact and the signs were probably due to an insufficiency of the apertures following myocardial weakness, or to the fact that the heart was held out by adhesions, rather than to true endocardial lesions.

The first patient presented was a girl, aged 6 years, who gave a history of sore throat and rheumatism in August. She had pronounced edema and all the other symptoms of acute heart failure on admission. As the best results with digitalis are not obtained when there is increased temperature, the digitalis was omitted on the seventh day and the child was placed on theobromin sodium salicylate, following which she immediately began to improve. The success with this drug in heart failure without pericarditis has been most gratifying.

Dr. Olmsted was interested in studying the absorption time in the cases of heart failurue, and in this patient the absorption time in the arm was shown to be considerably higher than that in the leg, which indicated that the circulation was better in the arms than in the more dependent portions of the body. The time was forty-four minutes in the arm and five minutes in the leg. This finding had been constant in all the heart patients thus far examined.

The second patient presented was a girl, aged 11 years, who had been admitted to the hospital with a history of attacks of paroxysmal tachycardia, which were typical of the attacks seen in the adult. Tonsillectomy was performed under local anesthesia about eight months ago. An attack of tachycardia

started at this time and continued for eleven days. The patient's condition remained good during the entire time and she made an uneventful recovery. For two months following this she had no attack. Since then, she has had three rather extensive attacks, each definitely associated with a nose and throat cold, but there had been decided improvement since the tonsillectomy and more freedom from attacks.

Only twenty-two cases of this nature are reported in the literature as occurring in children.

EDEMA. Presented by DR. C. A. ALDRICH.

Dr. Aldrich reported on the case of the girl he presented before the Society in 1923, who had had five attacks of generalized edema. Between these attacks she was normal, so far as could be determined by clinical or laboratory examination. Because he felt that she suffered from a recurrent intoxication rather than from kidney disease, in the course of an adenoidectomy, both antrums were opened. The day following this, her urine was free from albumin, whereas previously during weeks of hospital observation, it had contained much albumin (one-quarter inch ring). Following this procedure, she remained well for several months, but died of lobar pneumonia in September, 1924. At the time of death there was no edema.

He had hoped to present the patient shown, a boy, aged 3 years, as a case of edema which did not pit. The patient, however, developed a "cold" a day or so before presentation, and showed pronounced pitting with marked edema. He gave the following history: At 3 weeks of age he was christened, following which there was a generalized swelling which lasted two or three weeks. He had frequent colds, and three times had had attacks of generalized edema. On entrance, the edema was so marked that he could scarcely see. This attack cleared up, to be shortly followed by another. Both were associated with tonsillitis and otitis media. The urine constantly showed much albumin, many leukocytes, few casts and no blood. Blood chemical examination showed normal readings for the nitrogen elements, but a high cholesterol. There have been no uremic symptoms. The case was classed as one of nephrosis.

The patient, in contrast to the one previously reported, never had been normal while under observation. His tissues always contained an abnormal amount of fluid, but the skin did not always pit. In applying the intradermal salt solution test, it was found that whereas in normal skin the injected solution is palpable for over one hour, in his skin it disappeared in from thirty to forty minutes. It was thought from this that his tissues absorbed water more rapidly than normal. Dr. Aldrich was of the opinion that the intoxication which caused the edema persisted in a lesser degree between the attacks.

During the first attack, as the edema of the subcutaneous tissues subsided, the girth increased 3 inches due to increasing ascites. It was thought probable that the fluid freed from the skin and tissues accumulated in the serous cavities temporarily until the kidneys lost enough edema to eliminate normal amounts of urine.

The case was presented to illustrate that edema is not merely a complicating condition, but that it is a progressive process revealing in successive stages different clinical manifestations.

PATHOLOGICAL SPECIMEN AND REPORT. Presented by DRS. G. L. KAUFMAN and W. G. HIBBS.

The specimen was taken from a boy, aged 16 months. There was a history of pneumonia, clubbing of the fingers and spots resembling tuberculid. The Pirquet test was positive. The dulness was more marked anteriorly than posteriorly and there was a cavity at the nipple level. The child was admitted to the hospital weighing 20 pounds, but there was a temporary gain of 3 pounds. The temperature ranged from 99 to 102 F. The child was active

until two weeks before death, when he suddenly refused to eat and there was marked loss of weight. At that time the neck was rigid. Several lumbar punctures gave negative findings. Sugar varied from 85 to 92 mg., which spoke against tuberculous meningitis. Sputum examinations made by many different workers never showed any tubercle bacilli.

Dr. Hibbs presented the specimen of the right lung adherent to the chest wall, and the peribronchial and mesenteric glands. They had opened into one cavity which contained about 60 c.c. of thin, green, purulent material, in which a large number of acid fast bacilli were found.

DIPHTHERIA CARRIER. Presented by DR. T. C. GALLOWAY.

The patient was a girl, aged 2½ years, who had been a diphtheria carrier for ten months. The left maxillary sinus was shown to be the source of the diphtheria infection.

An antrum window was made. Cultures were positive one week later. Irrigation was done through the window daily for one week with surgical solution of chlorinated soda. After stopping for two days, two successive nasal cultures were negative.

DR. RUTH BOYNTON, of Minneapolis, spoke briefly of the status of the Shepard-Towner law and public health in a state wide way, and of the infant welfare work in Minnesota, stressing the point that all the work is being done with the cooperation and approval of the doctors throughout the state, most of it being carried on at the invitation of the physicians in each locality.

ST. LOUIS PEDIATRIC SOCIETY

Nov. 21, 1924.

GEORGE M. TUTTLE, M.D., *President*

THE OCCURRENCE OF MONGOLISM IN ETHIOPIANS. Presented by DR. ADRIEN BLEYER.

The first paper to attract attention to mongolism appears to have been that of Langdon Down in England, published in 1866. Since that time, the cases of mongolism reported have belonged, it seems, exclusively to the Caucasian races, a belief which is expressed in a review of the subject by Muir, which was made a few years ago. The recent report by Tumpeer in Chicago, however, of the occurrence of mongolism in a Chinese boy prompted the making of this additional report of its occurrence in the negro.

Three cases are reported, two in girls and one in a boy, who presented abundant evidence of this condition and in two of whom no history of any admixture of white blood could be obtained. The third, and for that matter all three, showed without any doubt that Ethiopian blood is no guarantee against mongolism, and it may occur in this race as well as in the white or probably any other.

SYMPTOMS OF SCARLET FEVER. Presented by DR. WISTAR WHITE.

This presentation consisted of clinical observations and case reports.

RECENT STUDIES ON ETIOLOGY AND IMMUNITY IN SCARLATINA. Presented by DR. J. V. COOKE.

The studies of Drs. A. R. Dochez, G. F. and G. H. Dick and other investigators briefly reviewed, and the explanation of the clinical phenomena of scarlatina in the light of these observations were discussed. Apparently two

distinct processes are involved in the infection. First, a true toxemia with local production by the scarlatinal streptococcus, of a soluble toxin which is absorbed and causes the rash, fever and possibly a specific toxic effect on the heart muscle and capillaries (nephritis). This toxin may be neutralized by antitoxin, either immune horse serum or serum from convalescent scarlatina patients, in the same manner as diphtheria toxin is neutralized by its antitoxin. The immunity to scarlatina furnished by an attack is apparently an immunity to this toxin. Second, there may be an invasion of the tissues (tonsillitis, angina) by the scarlatinal streptococcus, a pathologic process entirely distinct from the toxic action. This invasive action results in lesions and symptoms similar to other infections by pyogenic cocci and these lesions are not controlled by specific antitoxic serum.

Three case reports of toxic scarlatina with high fever were presented, which illustrated the markedly beneficial effect of scarlatina antitoxin on the fever rash and general toxicity, although the inflammatory foci showed no immediate effect of the serum and regressed rather slowly.

Post Scarlatinal Nephritis. Presented by Dr. A. F. Hartmann.

The incidence of nephritis accompanying or following scarlet fever averages about 20 per cent., varying widely with different epidemics. The lesions are not confined to the kidney, but are general and involve particularly the capillaries of the entire body. The most common type, that appearing the third or fourth week after the rash, probably results from the early injury done by the soluble toxin of the streptococcus of scarlet fever. Neither its incidence nor its severity is affected by administration of convalescent serum, which may be quite effective in reducing the toxicity and lowering the temperature during the early stage of the rash. In this way it is analogous to postdiphtheritic multiple neuritis. The less common type, that associated with the late severe anginas, is probably similar in origin but more intense, and certainly sometimes may be due to the actual invasion of the kidney substance by the streptococcus. Diet plays very little part in the incidence, but does have some bearing on the outcome. The prognosis in the more common type is very good. Treatment is not specific. Complete rest and low protein diet should be emphasized as a means of reducing the load on the capillaries of the body in general, and kidney (glomeruli) in particular.

Book Reviews

INFANTILE PARALYSIS IN VERMONT. STATE DEPARTMENT OF PUBLIC HEALTH, 1924.

This volume, Vermont's experience with infantile paralysis from 1894 to 1922, was prepared as a memorial to Dr. Charles Caverly, who as head of the Vermont State Board of Health, made several contributions to the study of this disease. As such, it serves not only as a history of one of the first epidemics experienced in this country, but as a tribute to Dr. Caverly's organization.

The papers are collected from various medical journals in which they appeared. Several of them present the well known contribution of Lovett and Martin's spring balance test as well as the first experiences with muscle training in the after-care of patients with poliomyelitis. The books ends with several communications dealing with the now familiar research with the virus of poliomyelitis and the early experiments with serum therapy.

SOCIAL HYGIENE OF INFANCY DURING THE FIRST YEAR. BY MLLE. LE DR. G. LABEAUME, Paris, Masson et Cie, 1924.

In this volume of 146 pages, Dr. Labeaume reviews the mortality rates for different periods of the first year, in France, and points out that the different methods of calculation in the various cities and departments render these statistics almost unserviceable. She also calls attention to the delay on the part of the authorities in publishing their reports, thus preventing frequent and fair comparisons among the communities interested.

As in other countries, poverty, ignorance and neglect are the factors chiefly concerned in the relatively high death rate now prevailing in France, which was the first to adopt (1874) a comprehensive law for the protection of infants.

Notwithstanding the further development of this act, as represented by the crèches, consultation de nourrissons, gouttes de lait, cantines maternelles, etc., France has not kept pace with other countries, notably England, New Zealand and the United States, in devising means and assembling material for combating the indefensible loss of life during the first year.

Among the subordinate causes of the great sacrifice all countries are making, Dr. Labeaume mentions permanent separation of mother from child, artificial feeding, tuberculosis, syphilis, insanitary houses and the pernicious effect of a rigorous climate. She shows what has been accomplished, both at home and abroad, in the fight against preventable disease and pleads for a better organization of federal and private forces in the amelioration of conditions surrounding child life among the poor.

Compulsory attendance on the new-born is demanded. Prenatal and postnatal clinics are suggested, with repeated medical examinations throughout the period of infancy. The monograph concludes with an exhaustive international bibliography.

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